Metals in Life or the Inorganic Chemistry of Life
Chemistry 2211a

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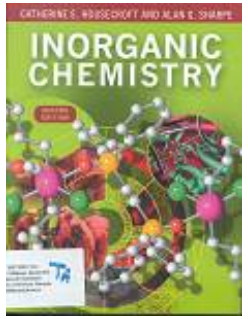
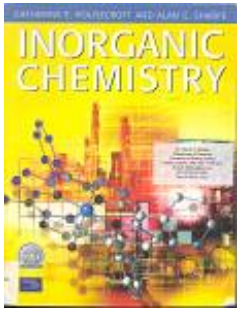
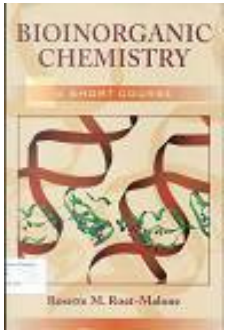
2) Important chemistry and special inorganic chemistry for bioinorganic chemistry

1. Periodic table
    a. Elements, transition metals, trends, electronic configurations, d orbitals
    b. Hard and Soft metals and Ligands
    c. Sizes of cations, atoms, anions; size to charge ratio
2. Metal-Ligand complex formation
    a. Special molecules that bind metals
        1. Ligands – special features of ligands
        2. Shapes of complexes
    b. Equilibrium constants
        1. K_F
        2. Chelate effect
        3. K's for multiple Ligands
        4. pK_a







(Check with "Late Breaking News" on URL instruct.uwo.ca/chemistry/2211a for changes.)
Note: B&W version is available for printing from "Download single file copy" link by Sept. 6th.

Recommended text Books

Principles of Bioinorganic chemistry by Lippard & Berg. TAYSTK QU 130.L765 1994 (On heavy demand (2-hour loan) at the Taylor Library and in the book store.)

Bioinorganic chemistry: a short course by Roat-Malone. QU130.R628b (On heavy demand (2-hour loan) at the Taylor Library and in the book store.)

Bioinorganic chemistry: inorganic elements in the chemistry of life: an introduction and guide by Kaim and Schwederski. (On heavy demand (2-hour loan) at the Taylor Library.)

The biological chemistry of the elements: the inorganic chemistry of life by da Silva and Williams. QU4.S586b 2001 (On heavy demand (1-day loan) at the Taylor Library)

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To start then

1. Periodic table
   i. Elements, transition metals, trends, electronic configurations, d orbitals
   ii. Hard and Soft metals and ligands
   iii. Sizes of cations, atoms, anions; size to charge ratio

Summary : This section provides the background necessary to understand the following scenarios:

1. Zn exists as the 2+ cation only and binds to sulfur in cysteine as well as to nitrogen in histidine but Na exists only as the 1+ cation and never binds to cysteines, rather preferentially to oxygen in water, and even better, to oxygen in carboxylic acids, the O^-.
2. The electronic configuration of each element and its place in the Periodic Table controls its chemistry.
3. For metals in Groups 3-12 (V – Zn) the key to the chemical properties is the arrangement of the 5 3d orbitals** and the electron distribution in the d-orbitals.
4. Equilibrium is a thermodynamic property that tells us energetically which way the reaction will go but not how fast.
5. The chelate effect is very important as biological reactions benefit from the enhancement in binding constant. Reaction rates tell us how fast the reaction takes place.

**By "arrangement", I mean the energy of each of the 5 3d orbitals when the metal is part of a complex – see slide 41.

L-B	R-M	K-S	In Housecroft 2nd ed.	Problems to do
1-2			See ch. 1, p 20-21; Ch. 20, p 557-564.	If blank – see later

3094b

The Periodic Table…

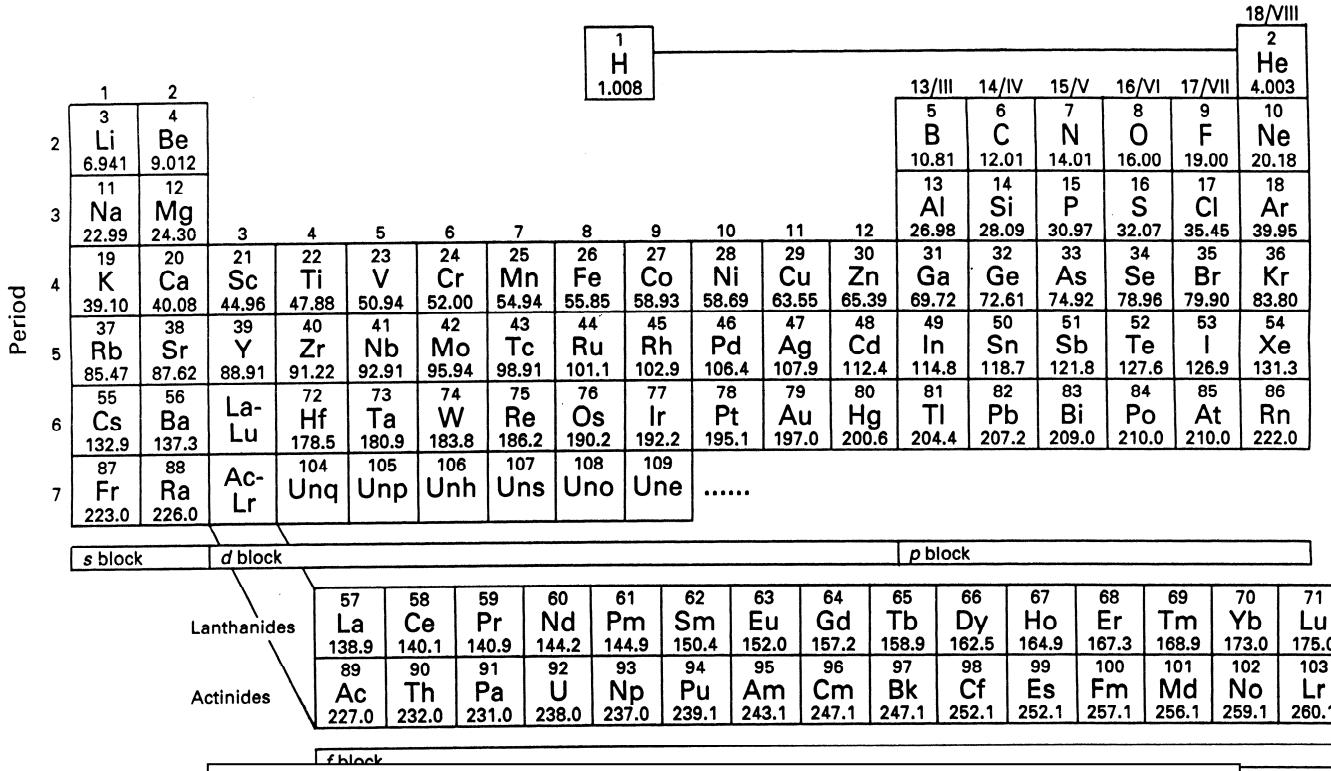
1. We know about Rows and Columns
2. Rows: Periods – generally the only link is the same (s, p) or 1 less (d) valence shell is being filled – so these elements are of similar size (always decreasing) BUT their properties are completely different.
3. The columns indicate the Atomic Orbital (AO) being filled 1 & 2 –s; 3-12 (d) (or (f)); 13-18 p
4. GROUPS – have numbers & names

Alkali metals (1) Alkaline earths (2)
Chalcogens (16), Halogens (17) (18)
Rare gases
All MAIN groups (13-18)

8. Groups 3-12 –d-block elements called either Transition Metals or d-block metals (dbMs) – see →
9. Major groups we will study (learn) 1, 2, 12, 17 + all the others see below…

So where are our key metals? Next slide

The Periodic Table



→ Why not all called Transition Metals? Well, the definition requires at least 1 d-electron. So, many oxidation states (which ones?) and Zn^{2+} don't fit. D-block metal (dbM) includes all elements groups 3-12.

Refresh your memory about the Periodic Table from your High School and 1st year notes and text books

Answer the following: Self-Study 3 & 4 – p 21 H-S
(config of O is? ……)
Number of unpaired electrons in Al is/are?)
Worked example 1.5 (config of Be and P). See Table 1.3 on p 18 of H-S and in many other 1st yr textbooks.

L-B	R-M	K-S	Problems to do
1-2			Check – Housecroft & Sharpe Inorganic Chemistry 2nd Ed – p 20 -

Electronic configurations
The Aufbau Principle.

We need to know the configurations of key biologically-important elements

Na, K, Mg, Ca, Fe, Co, Cu, Zn, O, N, S, P

The configurations of the free, gaseous neutral atoms are (the full list is on the next slide):

Na	O
K	S
Mg	N
Ca	P
Cr	Cu
Fe	Zn

But neutrally charged (=0) species are NOT found in biology, rather oxidized cations for metals and negatively charged anions for non-metals (other than C, N, P) - see next slides for the configurations of the cations common in biology

Table 1.3 Ground state electronic configurations of the elements up to $Z = 103$.

Atomic number	Element	Ground state electronic configuration	Atomic number	Element	Ground state electronic configuration
1	H	$1s^1$	53	I	$[Kr]5s^24d^{10}5p^5$
2	He	$1s^2 = [He]$	54	Xe	$[Kr]5s^24d^{10}5p^6 = [Xe]$
3	Li	$[He]2s^1$	55	Cs	$[Xe]6s^1$
4	Be	$[He]2s^2$	56	Ba	$[Xe]6s^2$
5	B	$[He]2s^22p^1$	57	La	$[Xe]6s^25d^1$
6	C	$[He]2s^22p^2$	58	Ce	$[Xe]4f^16s^25d^1$
7	N	$[He]2s^22p^3$	59	Pr	$[Xe]4f^36s^2$
8	O	$[He]2s^22p^4$	60	Nd	$[Xe]4f^46s^2$
9	F	$[He]2s^22p^5$	61	Pm	$[Xe]4f^56s^2$
10	Ne	$[He]2s^22p^6 = [Ne]$	62	Sm	$[Xe]4f^66s^2$
11	Na	$[Ne]3s^1$	63	Eu	$[Xe]4f^76s^2$
12	Mg	$[Ne]3s^2$	64	Gd	$[Xe]4f^76s^25d^1$
13	Al	$[Ne]3s^23p^1$	65	Tb	$[Xe]4f^96s^2$
14	Si	$[Ne]3s^23p^2$	66	Dy	$[Xe]4f^{10}6s^2$
15	P	$[Ne]3s^23p^3$	67	Ho	$[Xe]4f^{11}6s^2$
16	S	$[Ne]3s^23p^4$	68	Er	$[Xe]4f^{12}6s^2$
17	Cl	$[Ne]3s^23p^5$	69	Tm	$[Xe]4f^{13}6s^2$
18	Ar	$[Ne]3s^23p^6 = [Ar]$	70	Yb	$[Xe]4f^{14}6s^2$
19	K	$[Ar]4s^1$	71	Lu	$[Xe]4f^{14}6s^25d^1$
20	Ca	$[Ar]4s^2$	72	Hf	$[Xe]4f^{14}6s^25d^2$
21	Sc	$[Ar]4s^23d^1$	73	Ta	$[Xe]4f^{14}6s^25d^3$
22	Ti	$[Ar]4s^23d^2$	74	W	$[Xe]4f^{14}6s^25d^4$
23	V	$[Ar]4s^23d^3$	75	Re	$[Xe]4f^{14}6s^25d^5$
24	Cr	$[Ar]4s^13d^5$	76	Os	$[Xe]4f^{14}6s^25d^6$
25	Mn	$[Ar]4s^23d^5$	77	Ir	$[Xe]4f^{14}6s^25d^7$
26	Fe	$[Ar]4s^23d^6$	78	Pt	$[Xe]4f^{14}6s^15d^9$
27	Co	$[Ar]4s^23d^7$	79	Au	$[Xe]4f^{14}6s^15d^{10}$
28	Ni	$[Ar]4s^23d^8$	80	Hg	$[Xe]4f^{14}6s^25d^{10}$
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34	Se	$[Ar]4s^23d^{10}4p^4$	86	Rn	$[Xe]4f^{14}6s^25d^{10}6p^6 = [Rn]$
35	Br	$[Ar]4s^23d^{10}4p^5$	87	Fr	$[Rn]7s^1$
36	Kr	$[Ar]4s^23d^{10}4p^6 = [Kr]$	88	Ra	$[Rn]7s^2$
37	Rb	$[Kr]5s^1$	89	Ac	$[Rn]6d^17s^2$
38	Sr	$[Kr]5s^2$	90	Th	$[Rn]6d^27s^2$
39	Y	$[Kr]5s^24d^1$	91	Pa	$[Rn]5f^27s^26d^1$
40	Zr	$[Kr]5s^24d^2$	92	U	$[Rn]5f^37s^26d^1$
41	Nb	$[Kr]5s^14d^4$	93	Np	$[Rn]5f^47s^26d^1$
42	Mo	$[Kr]5s^14d^5$	94	Pu	$[Rn]5f^67s^2$
43	Tc	$[Kr]5s^24d^5$	95	Am	$[Rn]5f^77s^2$
44	Ru	$[Kr]5s^14d^7$	96	Cm	$[Rn]5f^77s^26d^1$
45	Rh	$[Kr]5s^14d^8$	97	Bk	$[Rn]5f^97s^2$
46	Pd	$[Kr]5s^04d^{10}$	98	Cf	$[Rn]5f^{10}7s^2$
47	Ag	$[Kr]5s^14d^{10}$	99	Es	$[Rn]5f^{11}7s^2$
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The configurations of the free, gaseous neutral atoms are:

Na [Ne] $3s^1$	O [He] $2s^2 2p^4$
K [Ar] $4s^1$	S [Ne] $3s^2 3p^4$
Mg [Ne] $3s^2$	N [He] $2s^2 2p^3$
Ca [Ar] $4s^2$	P [Ne] $3s^2 3p^3$
Cr [Ar] $4s^1 3d^5$	Cu [Ar] $3d^{10} 4s^1$
Fe [Ar] $4s^2 3d^6$	Zn [Ar] $3d^{10} 4s^2$

Generally write the unfilled orbitals last.

Neutral (=0) species are NOT found in biology, rather oxidized cations for metals and negatively charged anions for non-metals (other than C, N, P) - see next slides for the configurations of the cations common in biology

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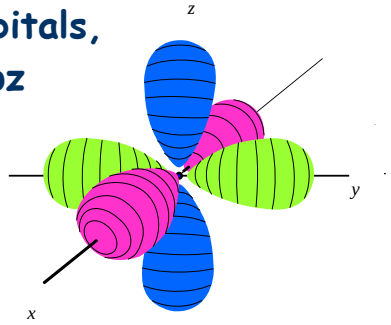
Atomic Orbitals –

s, p and d

We need to be able to draw them

The three 2p orbitals, 2px, 2py, 2pz



Initially, all 5 3d orbitals have the same energy, but we will see later how the 3d orbitals change their energies according to the geometry of the attached atoms (=ligands). So different coordination changes the chemical properties of the central metal, for example Fe(II) in deoxy- and oxymyoglobin.

See next page for different view of 3 d orbitals

L-B	R-M	K-S	Problems to do
31-35 – esp. but see later for the d-orbital splitting			Check H-S p 14 or s, p and d Do L-B p40 Qu. 1, 3

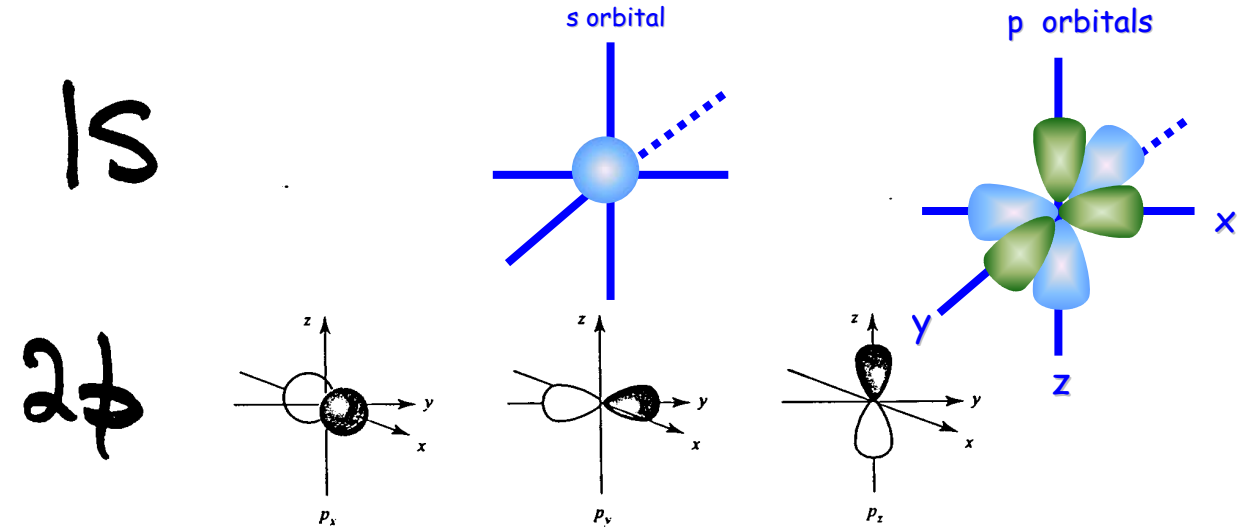
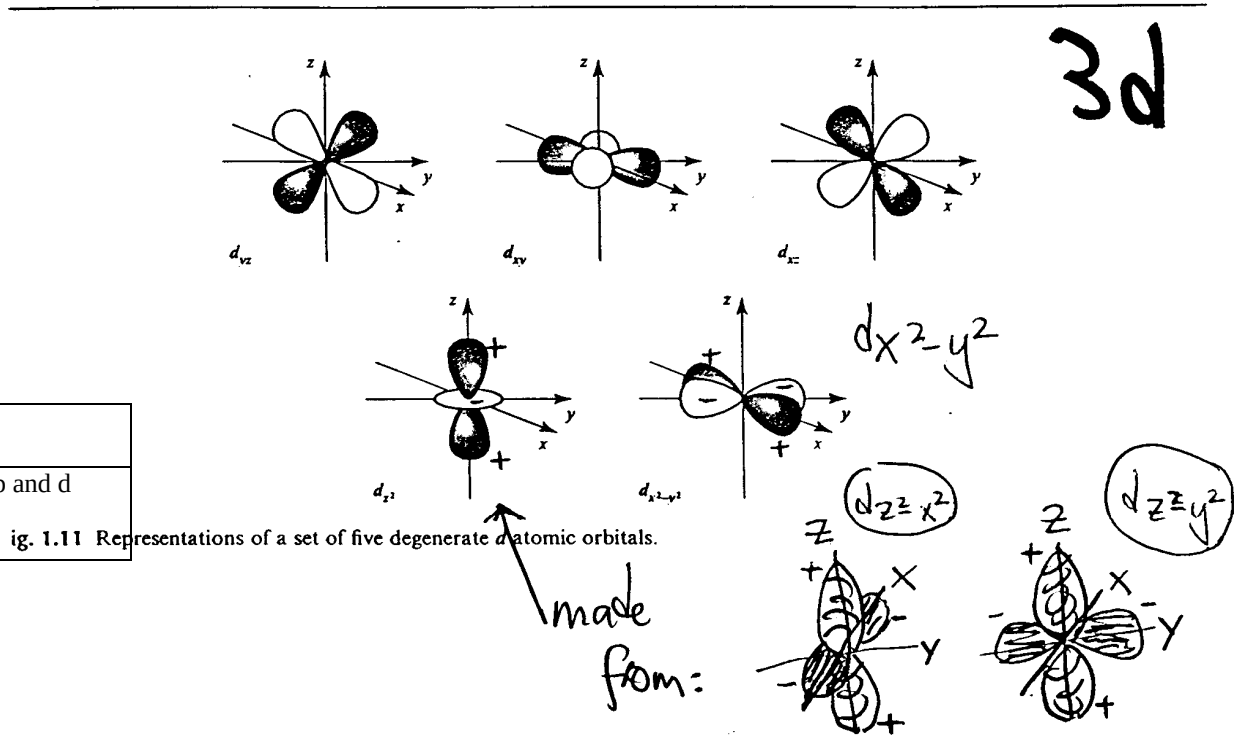


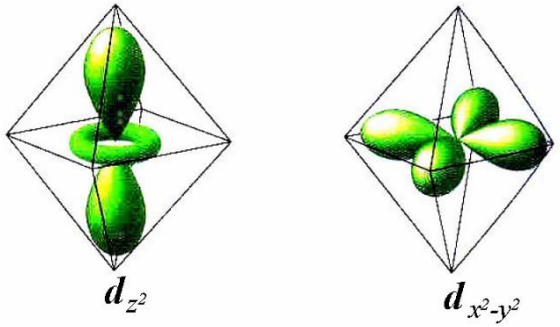
Fig. 1.10 Representations of an *s* and a set of three degenerate *p* atomic orbitals. The lobes of the p_x orbital are elongated like those of the p_y and p_z but are directed along the axis that passes through the plane of the paper.

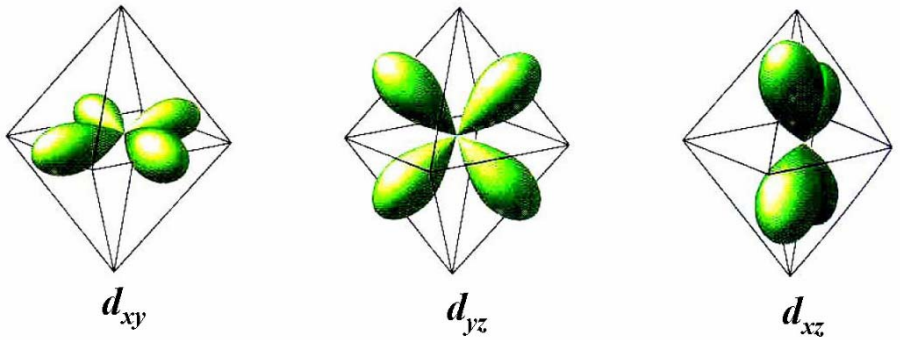


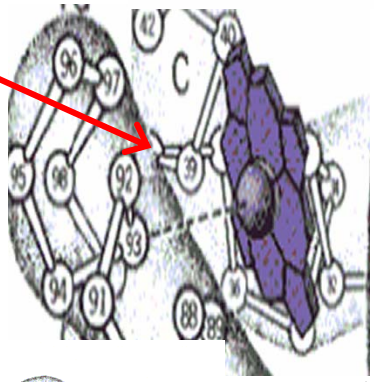
ig. 1.11 Representations of a set of five degenerate *d* atomic orbitals.

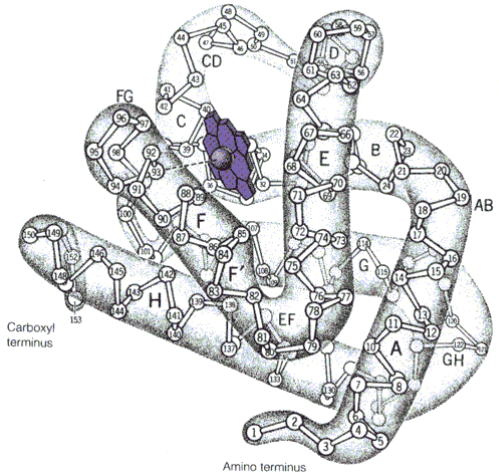
3d orbital arrangements –1 – the shapes of the 5 3d orbitals (2=the energies)

1. The lobes of the electron density in the 5 3d orbitals point at the vertices of the octahedron
2. The number of electrons in the 3d orbitals in each orbital and whether they are all the same spin (high spin) or paired up (low spin) changes the size of the cation.
3. Many dbM complexes form octahedral shapes (ML_6) the 3d orbitals will interact with those attached ligands – for example, look at the heme group in myoglobin – 6 ligands bind to the Fe^{2+}.
4. This is the basis of the dioxygen binding of myoglobin and hemoglobin because the energies of each 3d orbital (there are 5 here) can be different and depends on the ligand (or no ligand) attached. Here we have 4 the same – N's on the protoporphyrin IX ring (PPIX) or heme ring, 1 N from HisF8 or His93 histidine imidazole side chain, and 1 empty spot (the 6th position) for water, or dioxygen or CO – but tight because of HisE7.
5. To memorize – the 3d shapes and the alingment of His93 connected to the Fe – heme and the O_2 and CO in Myoglobin.
6. His F8, means 8th amino acid in helical coil F (6th). We will call it His93. meaning 93rd amino acid from the N-terminal. HisE7 is His64. So where is His E7?

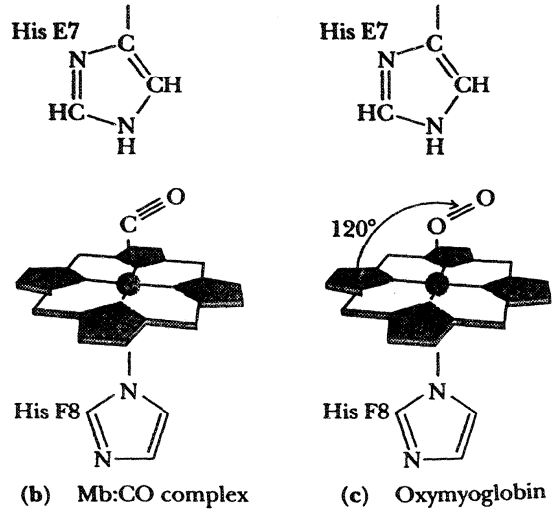








Find the 6 ligand s- 5 are N's, the 6th is the dioxygen – O_2 – see below RHS



The chemistry of metals depends on the loss of electrons.

1. Metals in most complexes, and in all biological complexes exist as cations (M^{n+}).
2. Cations form from ionization of 1, 2, 3 or even more electrons to form M^{n+}, where n = 1-7.
3. Electron rich neutral donor atoms and negatively charged anions around the metal stabilize the charge (electron-rich ligands coordinate metals to stabilize the +ve).
4. Consider MnO_4^- and NaCl (O^{2-} and Cl^-)
5. Because the IE of the d-block metals is similar they tend all to form M^{2+} cations (but also 1+, 3+ and 4+ in bio-mols).
6. Nature exploits this in Cu (2+ and 1+) and Fe (2+, 3+, 4+) complexes (how?).
7. The number of electrons that can be removed depends on sum(#e in 4s+3d).
8. So, we must be able to work out the electronic configuration of any element – for us that means up to Zn.
9. Do we have to learn this? Yes.

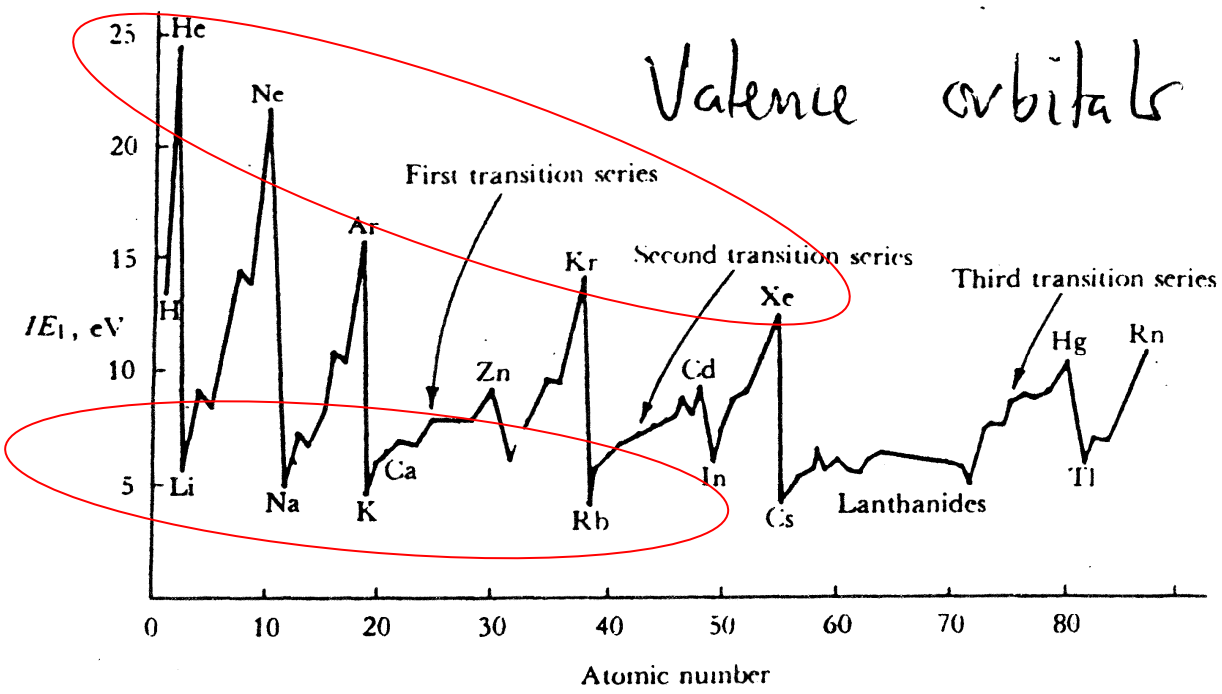


Figure 2-2 Variation of atomic ionization energy, IE_1, with atomic number. Notice that maximum ionization energies in a given row occur for the noble gases and that the ionization energies of the transition elements are similar.

POSSIBLE OXIDATION STATES	1+	2+	3+	4+
Fe		X	X	X
Co	X	X	X	
Cu	X	X		
Zn		X		
Always: the 4s electrons are emptied first				

Find complexes with Fe as Fe(II) and Fe(III from the later lectures and the text books. Which protein referred to in L-B uses Cu as both 1+ and 2+?
Charges on the metals and ligands?

L-B	R-M	K-S	Problems to do
			H&S p 24. Do Qu. 15, 19

3095

The chemistry of metals depends on the loss of electrons - oxidation.

1. Metals in most complexes, and in all biological complexes exist as cations.
2. Cations form from ionization of 1, 2, 3 or even more electrons to form M^{n+}, where n = 1-7.
3. Anions around the metal stabilize the +ve charge.
4. Consider MnO_4^- and NaCl (O^{2-} and Cl^-)
5. Because the IE of the d-block metals is similar they all form M^{2+} cations (as well as other ox states).
6. Nature exploits this in Cu and Fe complexes.
7. The total number of electrons that can be removed depends on Sum(4s+3d).
8. So, we must be able to work out the electronic configuration of any element – for us that means up to Zn.
9. Do we have to learn this? Yes – but specifically
10. IE of alkali metals is low & rare gases is very high..

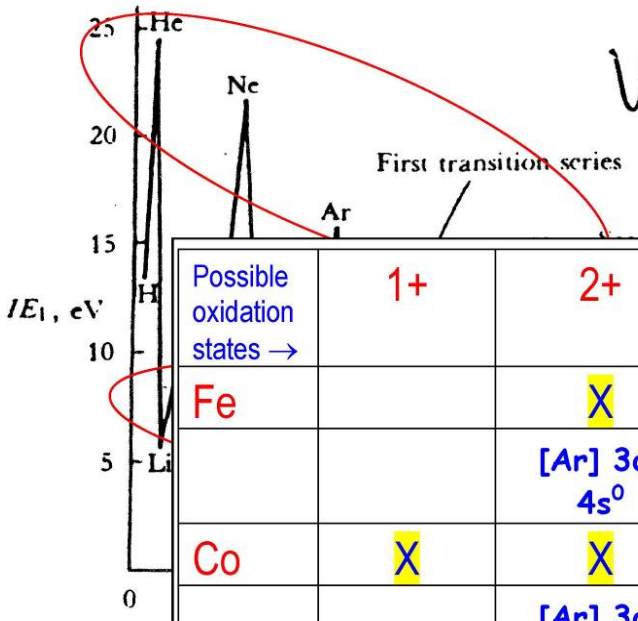


Figure 2-2 that maxim the ionizati

Possible oxidation states →	1+	2+	3+	4+
Fe		X	X	X
		[Ar] $3d^6$ $4s^0$	[Ar] $3d^5$ $4s^0$	[Ar] $3d^4$ $4s^0$
Co	X	X	X	
		[Ar] $3d^7$ $4s^0$	[Ar] $3d^6$ $4s^0$	
Cu	X	X		
	[Ar] $3d^{10}$ $4s^0$	[Ar] $3d^9$ $4s^0$		
Zn		X		
		[Ar] $3d^{10}$ $4s^0$		

ALWAYS – ALWAYS – THE 4s IS EMPTIED FIRST WHEN TRANSITION METALS OR dbMs ARE OXIDIZED (LOSE ELECTRONS)

Find complexes with Fe as Fe(II) and Fe(III from the later lectures and th text books. Which protein referred to in L-B uses Cu as both 1+ and 2+? Charges on the metals and ligands?

L-B	R-M	K-S	Problems to do
			H&S p 24. Do Qu. 15, 19

These are the metals that are found throughout biology and for which we know the oxidation state and some of the complexes that form.

For a metal complex, we need to know:

1) The oxidation state of the metal in the complex
2) The electronic configuration of this oxidation state
3) The electron distribution if this a dbM – we need to know which 3d orbitals the electrons occupy – to do this we need to know:
    a. The 3d splitting pattern for that geometry
    b. The ligand field strength(s)* of the ligands
    c. Determine whether the electrons are spin parallel or paired up (high or low spin)

*essentially the electron donor strength

Hard/ Int/Soft? Complete later	Preference for ligand donor group?	M	+1	+2	+3	+4	Example of molecules in biology	Example species where this molecule is found
		Na	+1				Nerves all cell membranes	all arganisms
		Mg		+2			Chlorophyll; ATP activation	Plants and all organisms
		K	+1				Nerves - cell membranes	All organisms
		Ca		+2			Muscle action – bone formation – shell formation	
		Sc						
		Ti						
		V		+2				
		Cr			+3		+6 – highly toxic +3 insulin production	humans
		Mn		+2				
		Fe		+2	+3	+4	Hemoglobin – myoglobin; +3 and + 4 catalase	mammals
		Co	+1	+2	+3		Vit B12 (CN^-)	All mammals
		Ni		+2				
		Cu	+1	+2			Hemocyanin – superoxide dismutase ($O_2^- \rightarrow H_2O_2$) Cytochrome oxidase	Invertebrates – lobsters, crabs – blue blood; mammals
		Zn		+2			Carbonic anhydrase (1 Zn per molecule)	mammals
		Cd		+2			+2 – toxic	
		Hg	0 and +1	+2			0 & +1 & +2 and methylated (CH_3Hg^+) – all toxic – worst is methylHg^+	
		Pb		+2		+4	+2 & +4 – both toxic	
		As			+3		+3 (& +5) – toxic	

So, what are the 'common' oxdation states of dbMs?

Oxidation Numbers of Elements in Their Compounds

1 1A												13 3A	14 4A	15 5A	16 6A	17 7A	18 8A
1 H +1 −1	2 2A																2 He
3 Li +1	4 Be +2											5 B +3	6 C +4 +2 −4	7 N +5 +4 +3 +2 +1 −3	8 O +2 +1 −1 −2	9 F −1	10 Ne
11 Na +1	12 Mg +2	3 3B	4 4B	5 5B	6 6B	7 7B	8	9 8B	10	11 1B	12 2B	13 Al +3	14 Si +4 −4	15 P +5 +3 −3	16 S +6 +4 +2 −2	17 Cl +7 +6 +5 +4 +3 +1 −1	18 Ar
19 K +1	20 Ca +2	21 Sc +3	22 Ti +4 +3 +2	23 V +5 +4 +3 +2	24 Cr +6 +5 +4 +3 +2	25 Mn +7 +6 +4 +3 +2	26 Fe +3 +2	27 Co +3 +2	28 Ni +2	29 Cu +2 +1	30 Zn +2	31 Ga +3	32 Ge +4 −4	33 As +5 +3 −3	34 Se +6 +4 −2	35 Br +5 +3 +1 −1	36 Kr +4 +2
37 Rb +1	38 Sr +2	39 Y +3	40 Zr +4	41 Nb +5 +4	42 Mo +6 +4 +3	43 Tc +7 +6 +4	44 Ru +8 +6 +4 +3	45 Rh +4 +3 +2	46 Pd +4 +2	47 Ag +1	48 Cd +2	49 In +3	50 Sn +4 +2	51 Sb +5 +3 −3	52 Te +6 +4 −2	53 I +7 +5 +1 −1	54 Xe +6 +4 +2
55 Cs +1	56 Ba +2	57 La +3	72 Hf +4	73 Ta +5	74 W +6 +4	75 Re +7 +6 +4	76 Os +8 +4	77 Ir +4 +3	78 Pt +4 +2	79 Au +3 +1	80 Hg +2 +1	81 Tl +3 +1	82 Pb +4 +2	83 Bi +5 +3	84 Po +2	85 At −1	86 Rn

This page **Not to be memorized – interest only**

3093

Atoms and ions are all different sizes cations are smaller than atoms and anions larger larger than the neutral atom.

Trends are important:

Down the groups – larger

Across rows: different trends not so easy to generalise.

This diagram shows how the 2+ cations are much smaller than the 1+ cations and how large the anions are.

Increasing the positive charge 1+ to 2+ to 3+ results in cations that are smaller and smaller – eg Na^+ to Mg^{2+} to Al^{3+}.

The size to charge ratio is important in biological coordination chemistry

Biological ligands recognise metals often by the size/charge ratio alone!

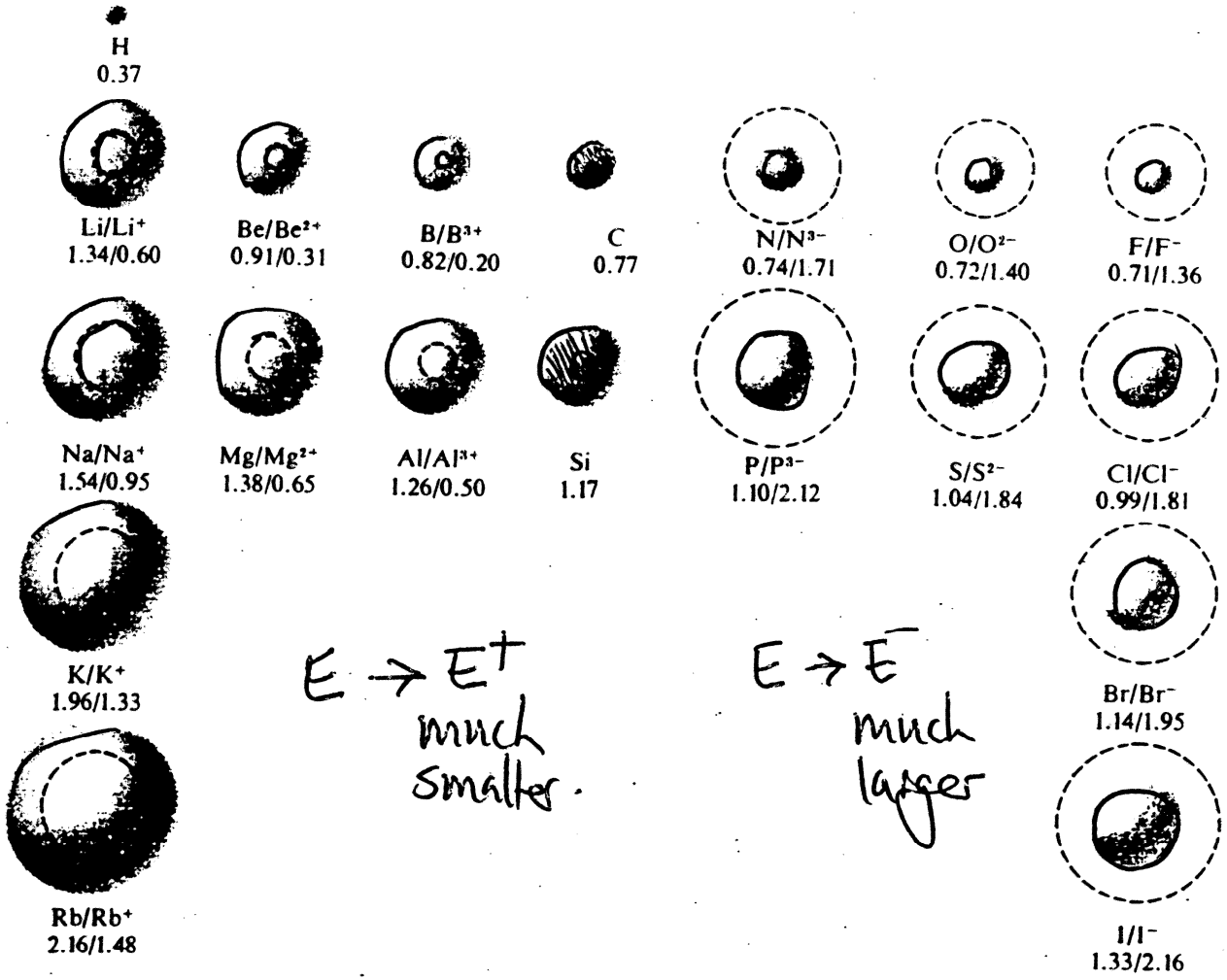


Figure 2-1 Relative atomic radii of some elements compared with the radii of the appropriate closed-shell ions. Radii are in angstroms. Solid spheres represent atoms, dashed circles represent ions. Notice that positive ions are smaller than their neutral atoms and that negative ions are larger.

Comparison of cations and anions

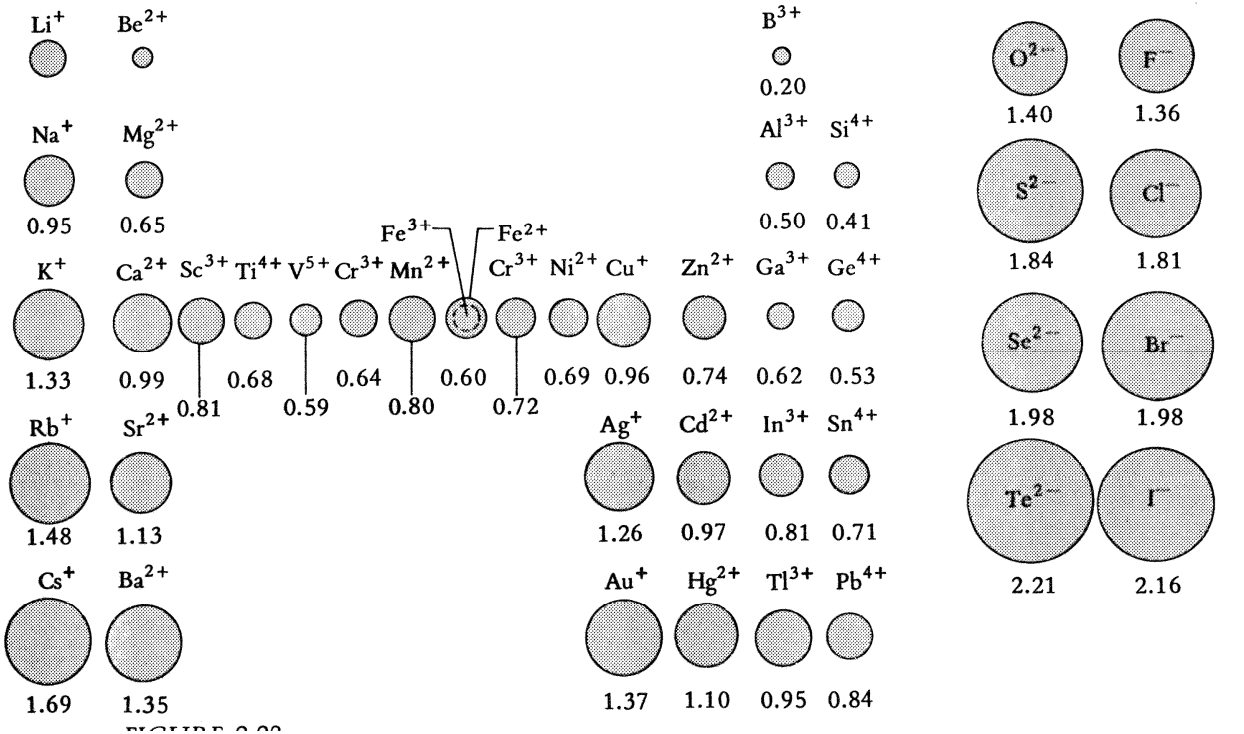
We can identify the biologically important elements from Group 1 and 2 , dBM and Group 13, 14, 16 and 17.

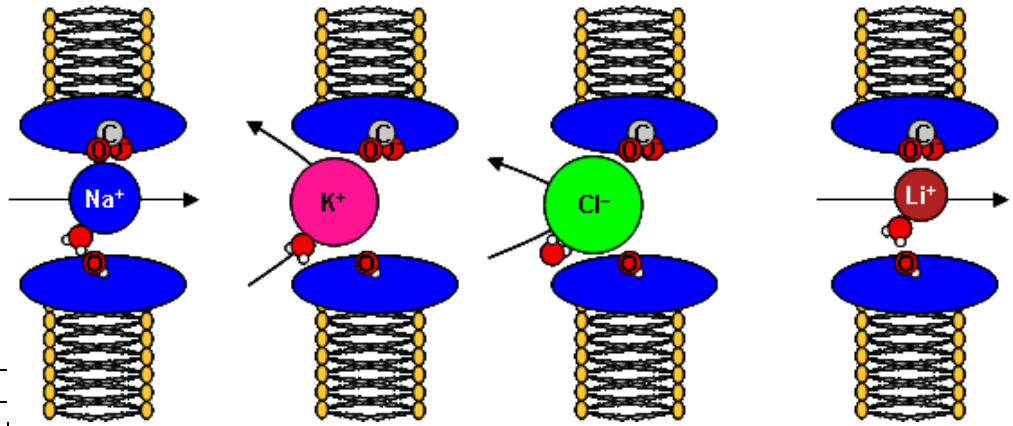
Trends:

1. Down the groups – always larger whether neutral, cation or anion because of the extra protns and neutrons and core electrons.
2. Across rows: different trends not so easy – track the 1st IE - high IE=smaller.
3. The greater the positive charge = smaller; negative charge = larger.
4. So Ca^{2+} is smaller than ……
5. And S^{2-} is larger than ……..
6. BUT d-block metals (dBM) all about the same.

This fig also emphasizes that isomorphous replacement can take place – substitute one cation for a cation of the same size – Pb^{4+} for Ca^{2+}.

Needs hard-soft rules followed though. So less likely to substitute Cd^{2+} for Ca^{2+} - why not? (See below)





L-B	R-M	K-S	Problems to do
1-2, 4-5		Table 2.7, p 27	Consider the charge/radius ratios – the large the radius the smaller the effect of charge. Also, consider the effect of removing or adding just 1 electron when there are only a few protons, ie Z<18 – much greater % effect

This is a description of how an enzyme pump that pumps 2 K^+ into a cell and pumps 3 Na^+ out of a cell works. This is a 'passive' mechanism. We will see more complex mechanism in the Biology unit (section 3). See also the cyclic polyethers and the antibiotics – valinomycin as synthetic examples of ion selectivity based on size.

We will describe the reasons coordination compounds form and the properties in the next several slides.

1) What are the key properties of LIGANDS?
2) Hard and Soft – explains why
3) What are the typical biological ligands? First amino acids that bind metals
4) Then, the compound has shapes, any in particular?
5) Why are dbMs so important? The 3d orbitals – they change their energies
6) Can we tell this happens? Yes, from the colours and magnetism of the compounds
7) Then we need to look at the binding constants – what pushes ligands and metals together - energy

Making compounds (1): a refresher

1. Simple liquids and solids involved neutral atoms and homonuclear diatomic molecules: Ar, He, N_2 and O_2 – here induced dipole moments allow for solutions and solids. These boil at low to very low temperatures reflecting the weak interatomic/intermolecular forces.

2. Next are salts – electrostatic interactions hold everything together --- Na^+ Cl^- salt is the quintessential example - in the solid a lattice of cations and anions – in solution, isolated – aquated ions. Very strong electrostatic bonds in crystals – melt at high temperatures.

3. Then molecules. Molecules involve bonds – that is electron sharing – an "electrostatic sandwich" M+--ee—L(now+).

There are different ways to account for the sharing: the simplest way is via Lewis dots .. O::O or O=O. We mean a bond forms – each bond has 2 electrons in it.
In these compounds each atom contributes electrons according to its electronegativity. The more electronegative the more electrons donated to the metal complex: the metal is a cation (no spare electrons), the ligand is an anion or electron rich (donates all electrons for the bond – usually 2).

In biological molecules, we will find special macromolecular, giant structures called secondary, tertiary and quaternary structures, these are formed by the biological molecule folding – the folding is held together by weak – electrostatic bonds (+…-), weak dipole moments (RRC=O) and most of all hydrogen bonds (ROH…$^-$OOCR). These weak bonds are fragile, and salt and heat can break them … the native protein is now denatured (think of egg white). The shapes formed by this folding are very stable because there are so many weak bonds. The shapes in many cases control the biological function completely.

How do elements form compounds? Well, they form coordination compounds with ligands 2

What's a coordination compound? Why do we need to know about them?

A coordination compound in biology, sometimes called a coordination complex, contains a central cationic metal ion (a metal which has lost 1, 2 … n electrons) surrounded by a number of negatively charged ions (single atoms or complex anions) or neutral molecules (which possess lone pairs of electrons) which are known as ligands.

We will also introduce the term Lewis acid and base for the metal and ligands, respectively, below (but remember the name now AND that metals accept electrons, ligands donate electrons).

If a ligand is capable of forming more than one bond with the central metal atom or ion, then ring structures are produced which are known as chelate compounds, the ring forming groups are described as chelating agents or polydentate ligands.

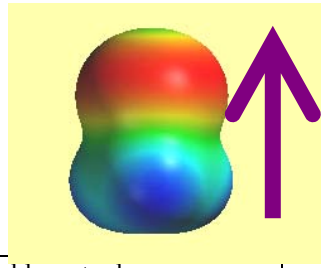
The coordination number of the central metal atom or ion is the total number of sites occupied by ligands. Note: a didentate ligand uses two sites, a tridentate three sites etc. – ok – so we need a list …

We need to return to the Periodic Table to highlight the atoms most likely to attach themselves to metals in biological systems

Remember

- the electropositive elements – ATTRACT ELECTRONS = METAL CATIONS
- electronegative elements – DONATE ELECTRONS = LIGANDS
- results in dipole moments and bonding → shared electrons

eg $CH_2=O$



Now to ligands …

L-B	R-M	K-S	Problems to do
22			If blank – see later

The Periodic Table

More POSITIVE

More NEGATIVE

	1	2											13/III	14/IV	15/V	16/VI	17/VII	18/VIII
	1 H 1.008																	2 He 4.003
2	3 Li 6.941	4 Be 9.012											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
3	11 Na 22.99	12 Mg 24.30	3	4	5	6	7	8	9	10	11	12	13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.07	17 Cl 35.45	18 Ar 39.95
4	19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.88	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.39	31 Ga 69.72	32 Ge 72.61	33 As 74.92	34 Se 78.96	35 Br 79.90	36 Kr 83.80
5	37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.94	43 Tc 98.91	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
6	55 Cs 132.9	56 Ba 137.3	La-Lu	72 Hf 178.5	73 Ta 180.9	74 W 183.8	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po 210.0	85 At 210.0	86 Rn 222.0
7	87 Fr 223.0	88 Ra 226.0	Ac-Lr	104 Unq	105 Unp	106 Unh	107 Uns	108 Uno	109 Une	.....								

Period

s block | d block | p block

Lant

Acti

Table 1.3 The Electronegativities of Selected Elements[a]

IA	IIA	IB	IIB	IIIA	IVA	VA	VIA	VIIA
H 2.1								
Li 1.0	Be 1.5			B 2.0	C 2.5	N 3.0	O 3.5	F 4.0
Na 0.9	Mg 1.2			Al 1.5	Si 1.8	P 2.1	S 2.5	Cl 3.0
K 0.8	Ca 1.0							Br 2.8
								I 2.5

increasing electronegativity

increasing electronegativity

[a]Electronegativity values are relative, not absolute. As a result, there are several scales of electronegativities. The electronegativities listed here are from the scale devised by Linus Pauling.

Special molecules that bind metals

Ligands – special features of ligands

1. Control the function of the metal
2. Change the shapes of complexes
3. There is an effect of shape on the energies of 3d orbitals (dbM's)
4. Equilibium reactions – the equilibrium constant, K_B
5.

Ligands – special features of ligands

(i) Biologically important ligands

N- (as $R_2N:$)

S- (as RS:R and RSH and RS^-)

O- containing (as RC=O:, RO:R, ROH, and esp RO^-)

and also water

OK – let us look at a typical small complex

(ii) Chelating ligands used to detoxify metals

BAL - soft (S)

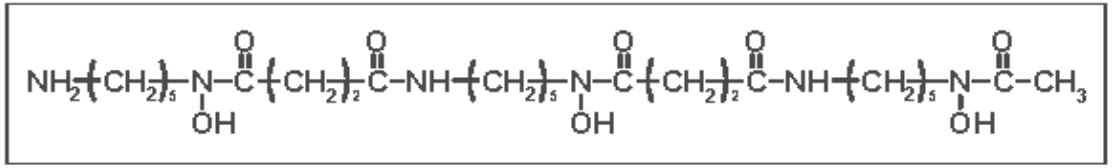
D-penicillamine – medium (N)

EDTA – hard (O)

Desferrioxamine B see LB p 13-14 – hard (O)

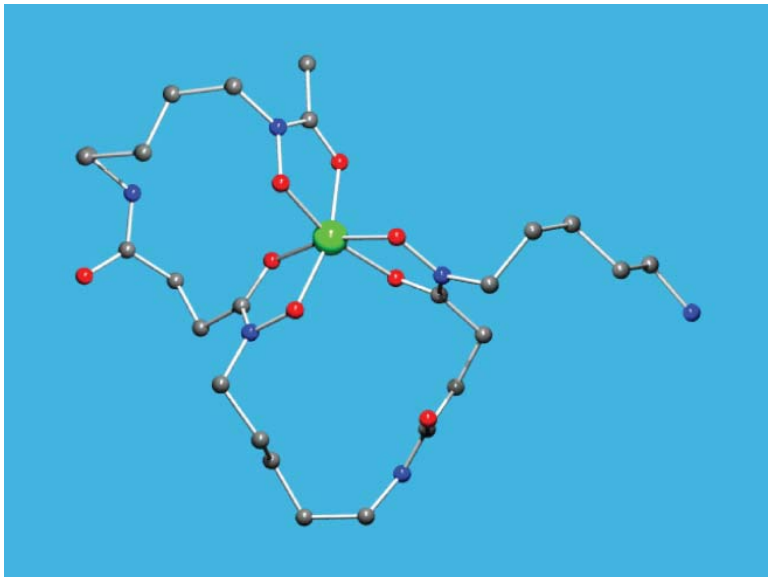
(All these structures coming up in 5 pages)

And note – later in "Chelators" in "Toxic Metals"



Desferrioxamine

Desferrioxamine B complex with Fe(III) used to remove excess iron in humans – a hexadentate chelator



L-B	R-M	K-S	Problems to do
21-23 32-33 45-46	Match ligands to the atoms listed in Table 1.7, p 6 4-5	P 13-28 – esp. p 13 & 14 14 15-36; esp p 27 – effect of radii on complex formation	Which ligand do you predict will bind to – Cu+ and Na+ Find structures for each of the ligands mentioned in the detoxifying section

Some examples – and further definitions and insight into the world of coordination complexes before we return to the biological examples (on the next slide)

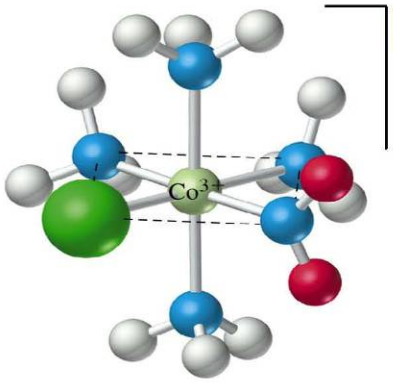
1) This coballt(III) complex, could write Co^{3+}, 3+ charge, so the electronic configuration starting at [Ar] is? .....

OK easier – choose the correct answer ---

Is it -[Ar] $4s^2$ $3d^7$; [Ar] $3d^7$; - [Ar] $4s^2$ $3d^4$; [Ar] $3d^6$?

2) The ligands are all ammonias NH_3 – neutral Lewis Bases.

3) The shape is octahedral (OCT) – see the slide below for a list of shapes – a very common shape for dbMs (actually, if you choose M^{2+} as an example, and use 6 waters as the Lewis Base ligand, probably a good bet, the complex will be OCT in shape.

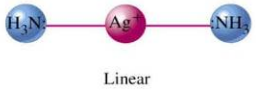


This is a complex between ammonia molecules, the Lewis base, the Co^{3+} is the Lewis acid, note, the overall charge of the complex is also + because ligands are not charged.

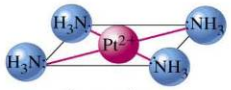
Three different ligands here – Cl^-, H_2O and NH_3.

So the overall charge of the complex is?

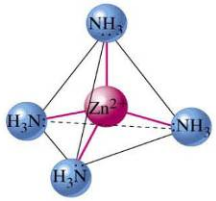
Add the number before the "+"



Linear



Square planar



Tetrahedral

The charges will be? Add the top half bracket and the correct charge to these images

And the configurations if the metal cations are Ag^+, Pt^{2+}, and the Zn^{2+}, are?

...
...
...

Are there any systematic ways of predicting which metal binds to which ligand?

In synthetic chemistry, it's not too easy – change the conditions and almost any ligand will coordinate any metal, BUT in biology, nature took the easy way out most of the time, or, why take chances and – take the easy route and react ligand sand metals that always react together…

Hard acid – Soft base theory

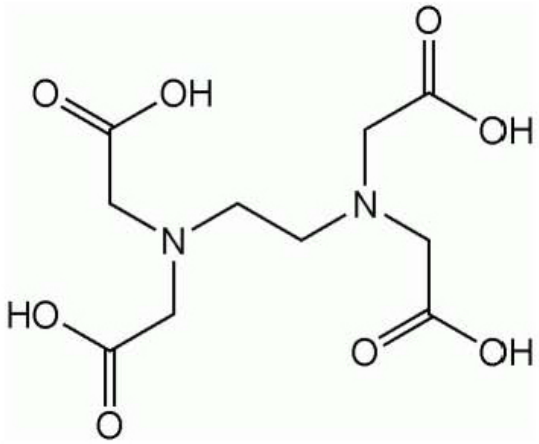
Hard acids react with hard bases and

Soft acids react with soft bases

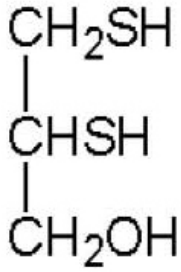
And intermediate acids and bases? Well, they react with everything.

Extremes – very hard, why?

Very soft, why?



$EDTAH_4$



BAL

3103

Hard-Soft Metals and Ligand atoms

1. Pearson Hard-Soft (Acid-Base) theory applied to metals and ligands – a critically important aspect of biological metal-based chemistry
2. Ca … Mg…
   Co… Cu ..
3. But, Cu^{+} and Hg^{2+} are really soft
4. So bind preferentially with ?
5. Although the metals are the same in biology, the ligands include amino acid side groups – come back to here once we have covered the amino acid section and add in the amino acids that bind metals –
6. remembering that uncharged N is intermediate, so binds all metals.

Table 2. *Classification of Hard and Soft Acceptors and Donors [3]*

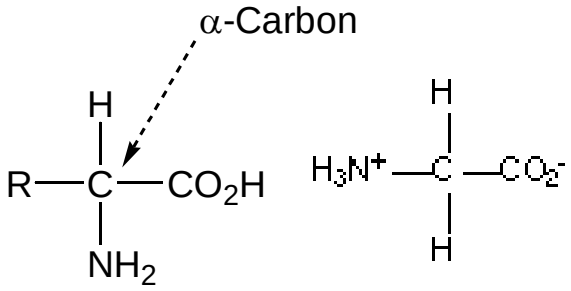
Acceptor		
Hard	Intermediate	Soft
H^+, Na^+, K^+, Be^{2+}, Mg^{2+}, Ca^{2+}, Mn^{2+}, Al^{3+}, Cr^{3+}, Co^{3+}, Fe^{3+}, As(III)	Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Pb^{2+}	Cu^{+}, Ag^{+}, Au^{+}, Tl^{+}, Hg^{2+}, CH_3Hg^{+}, Cd^{2+}
Donor		
Hard	Intermediate	Soft
H_2O, OH^-, F^-, Cl^-, PO_4^{3-}, SO_4^{2-}, CO_3^{2-}, O^{2-}	Br^-. NO_2^-, SO_3^{2-}	HS^-, S^{2-}, RS^-, CN^-, SCN^-, CO, R_2S, RSH Cys Met

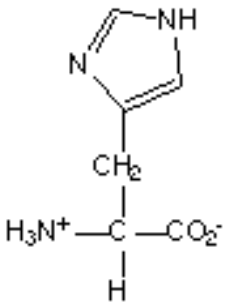
L-B	R-M	K-S	Problems to do
21-23; 24-25	Table 1.7, p 6	P 15; also 13-20 generally	Which metals do you predict will bind to metallothionein? See Fig 2.1 in L-B – why – search the web – what other metals bind to metallothionein??

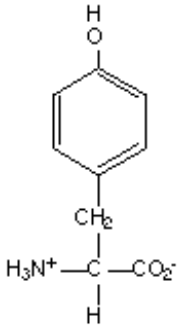
Biological Ligand molecules

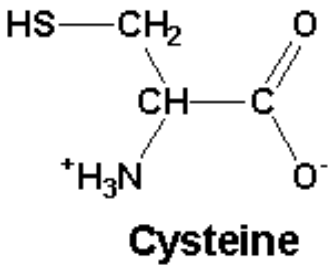
Excellent source for information http://en.wikipedia.org/wiki/List_of_standard_amino_acids

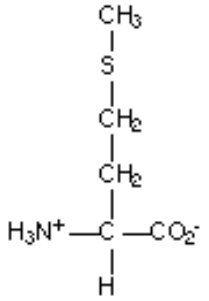
We'll jump ahead by bringing in those amino acids likely to bind metals as well here.











GLYCINE HISTIDINE TYROSINE CYSTEINE METHIONINE

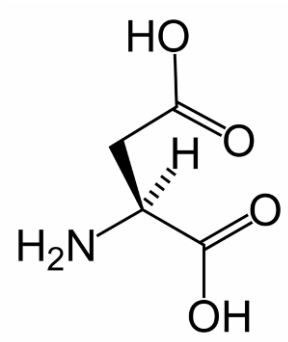
HIS - imidazole group N TYR O CYS S MET S

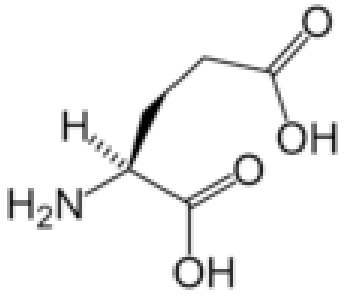
Oxygen from Asp – aspartic acid and Glu, glutamic acid

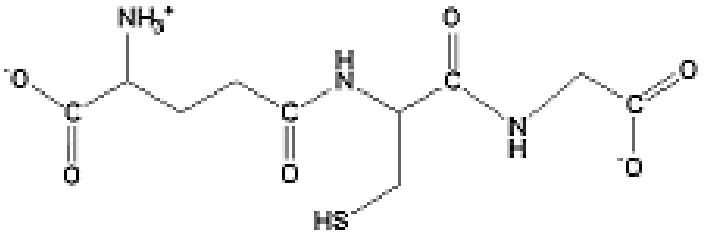
Which are the donor atoms?

Hard, Int or Soft?

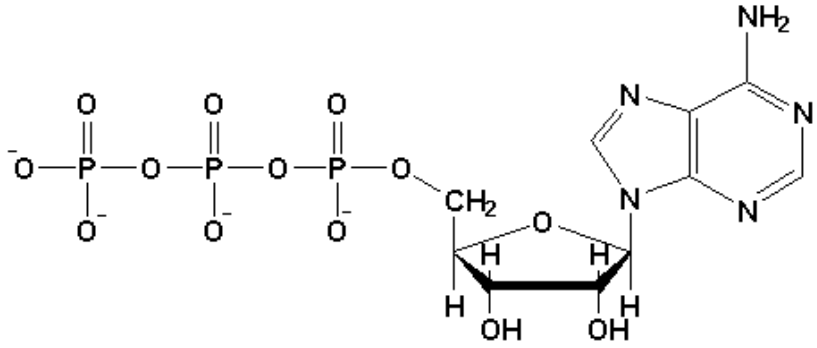
Then there are these biological ligands:







Glutathione



Adenosine triphosphate (ATP)

L-B	R-M	K-S	Problems to do
22 44; 46; 47		15-16; 16-38 everything about ligands,and metals, and rings; also 3d splitting	If blank – see later

3105

Structural form of the metal changes the function (from before)

1. Coordination by **ligands** – ligands are either neutral with nonbonding pairs (like NH_3) or anions like OH^- to stabilize the metal cation.
2. The more oxidized the metals, the more anionic the ligands have to be.
3. Biological LIGANDS – see after Hard-Soft slide – we must relate Hard-Soft character to the metal cation and the ligand

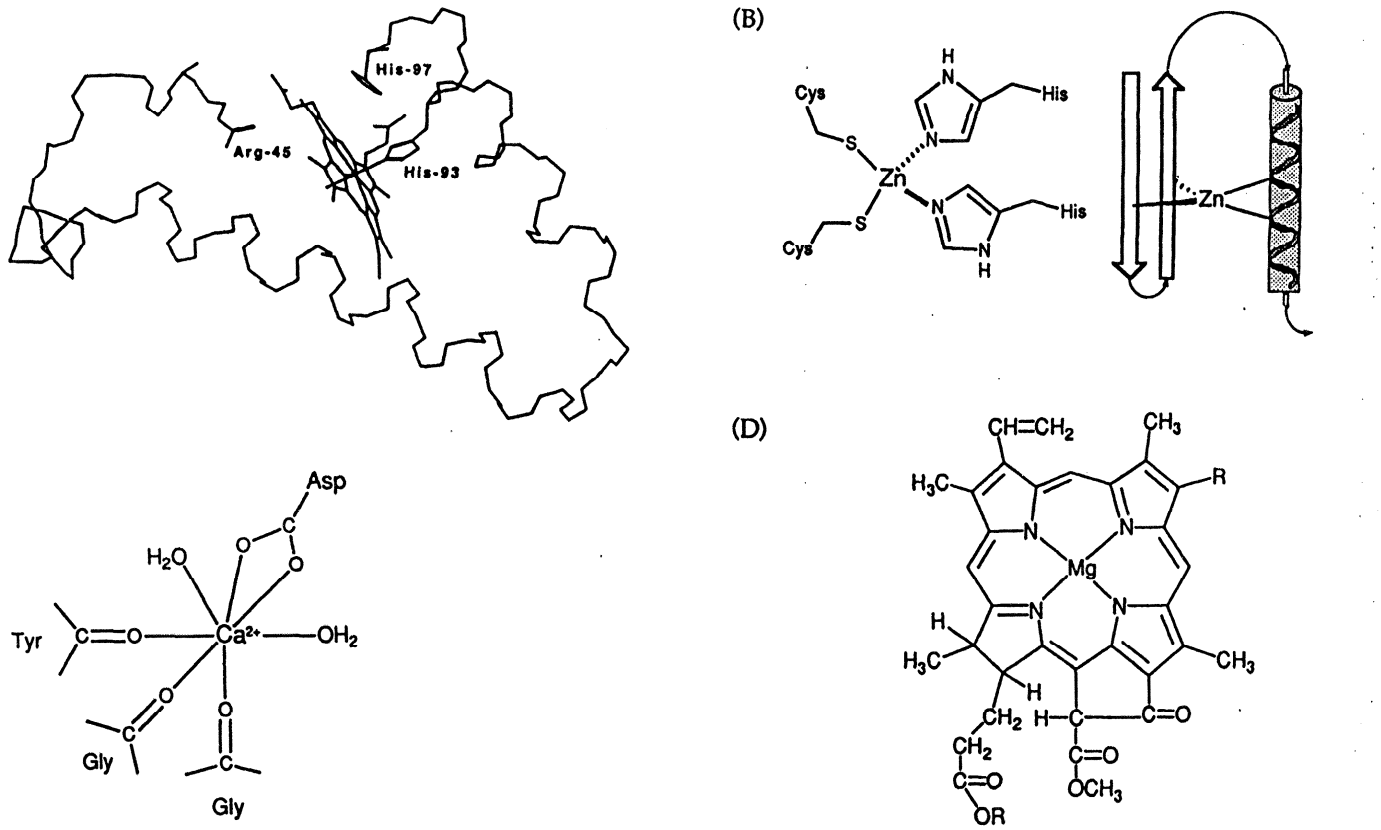


Figure 1.15 Coordination modes for metal binding to metalloproteins and peptides. (A) The heme prosthetic center and a portion of the backbone in myoglobin. (B) Bound Zn^{2+} in a zinc finger. On the right the portion of the protein backbone that forms the "finger" is traced. Figure 1.19 gives more details on such schematic diagrams. (C) The metal-binding domain of a Ca^{2+}-activated enzyme (phospholipase A_2) showing coordination of a chelating carboxylate, two water molecules, and three backbone carbonyls. (D) Chlorophyll from the light-harvesting complex of the photosynthetic reaction center.

What are the ligands – the atoms next to the metals in these examples? Write out the molecules without the metals in B, C and D. You'll need to check your biochemistry book for the amino acids – also coming in 3 lectures here.:

L-B	R-M	K-S	Problems to do

Why do we need to know about the properties of ligands?

Other than to understand how natural compounds maximise the functional power of metals, what about chelation therapy →

Ligands – special features of ligands (see Hard-Soft table below)

(i) Biologically important ligands

N- S- O- containing – esp O^- But also water

(ii) Chelating ligands used to detoxify metals

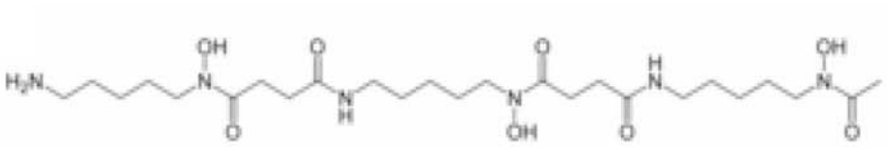
BAL - soft (S) invented to undo the damage of Mustard Gas – Lewisite →

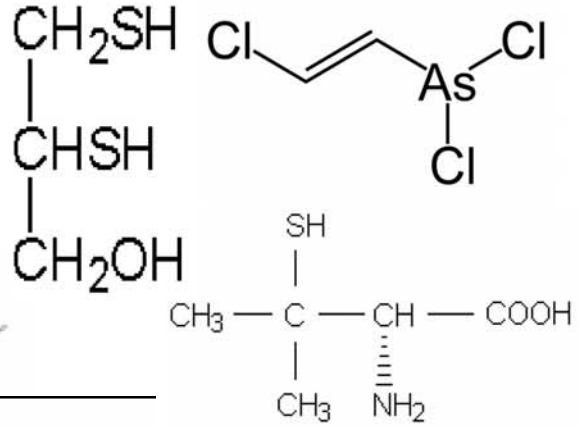
D-penicillamine – medium (N) Cuprimine, Depen – used to treat Wilson's Disease

EDTA – hard (O)

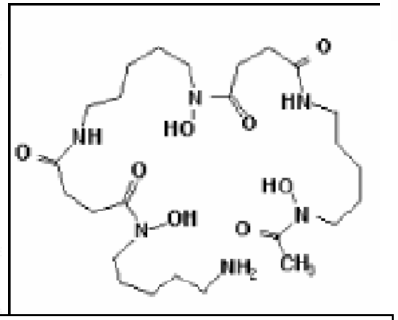
Desferrioxamine B

Desferal C - see LB p 13-14 – hard (O)

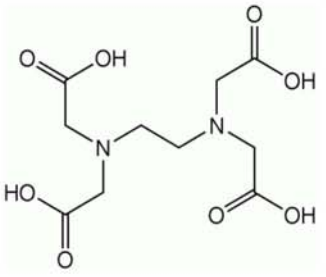




L-B	R-M	K-S	Problems to do
21-23 32-33 45-46	Match ligands to the atoms listed in Table 1.7, p 6 4-5	P 13-28 – esp. p 13 & 14 14 15-36; esp p 27 – effect of radii on complex formation	Which ligand do you predict will bind to – Cu+ and Na+ Find structures for each of the ligands mentioned in the detoxifying section

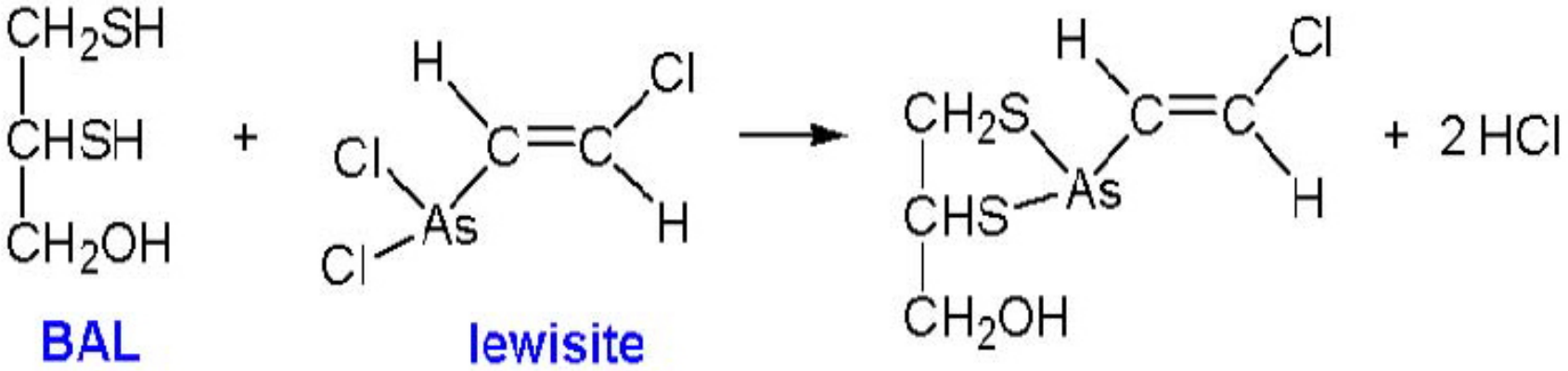


Desferrioxamine B – 6 oxygens bind 1 Fe(III) ion



1. An agent frequently used in chelation therapy is dimercaprol (also known as BAL or British Anti-Lewisite). Oral chelating agents used as alternatives to BAL are 2,3-demercaptosuccinic acid (DMSA), dimercaptopropanesulfonate (DMPS),
2. D-penicillamine
3. Desferrioxamine B often used to chelate iron.
4. Ethylenediamintetraacetic acid (ETDA) also has an affinity for lead and was one of the first chelators developed.

So, how does BAL work with Lewisite?

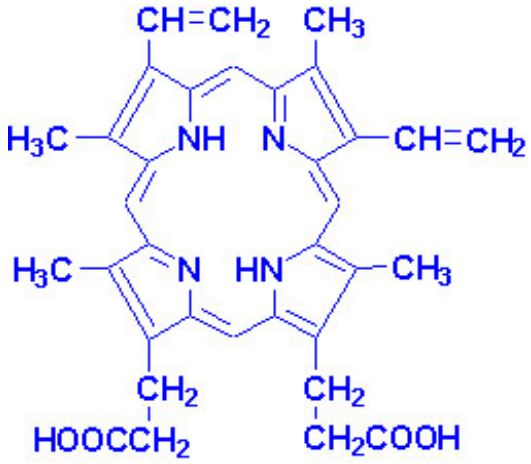


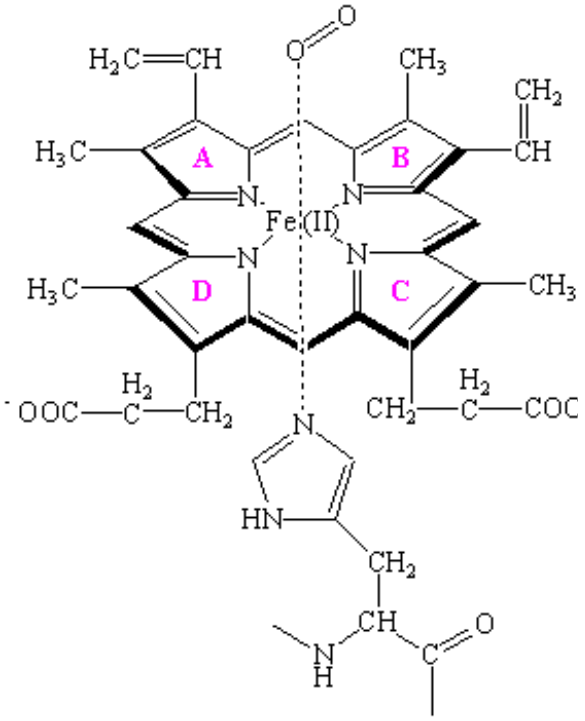
BAL lewisite

Chelation in action …. Didentate attachment of the BAL to the As

Some of the many different Porphyrin rings in biology - see LB 131

freebase protoporphyrin -see next slide how to memorize



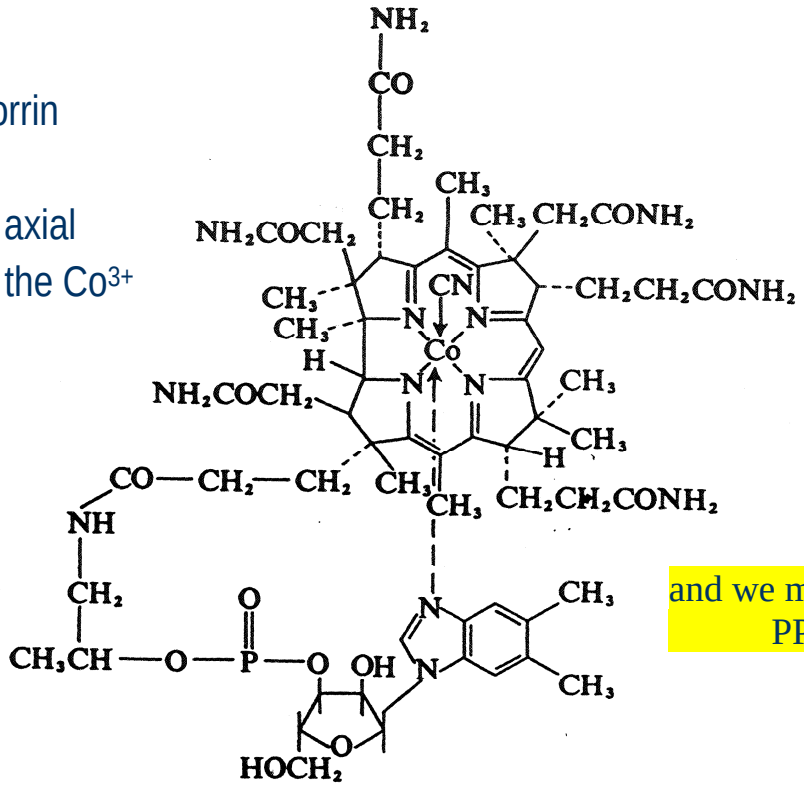


Heme= iron protoporphyrin IX

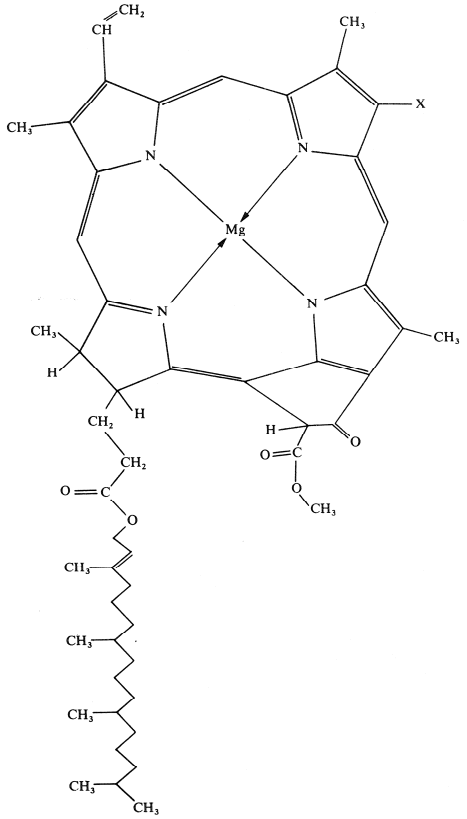
IX

Cobalt Corrin
Vit B12
Note CN^- axial ligand on the Co^{3+}

1150 ..

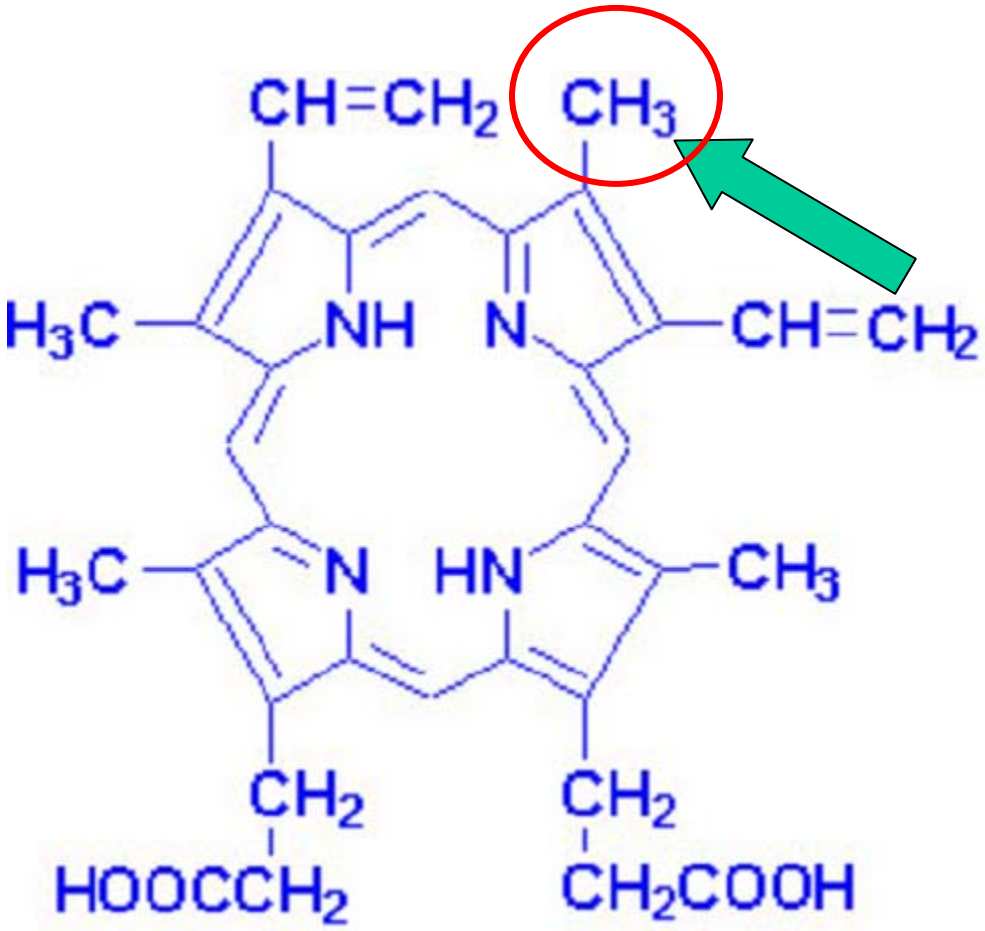


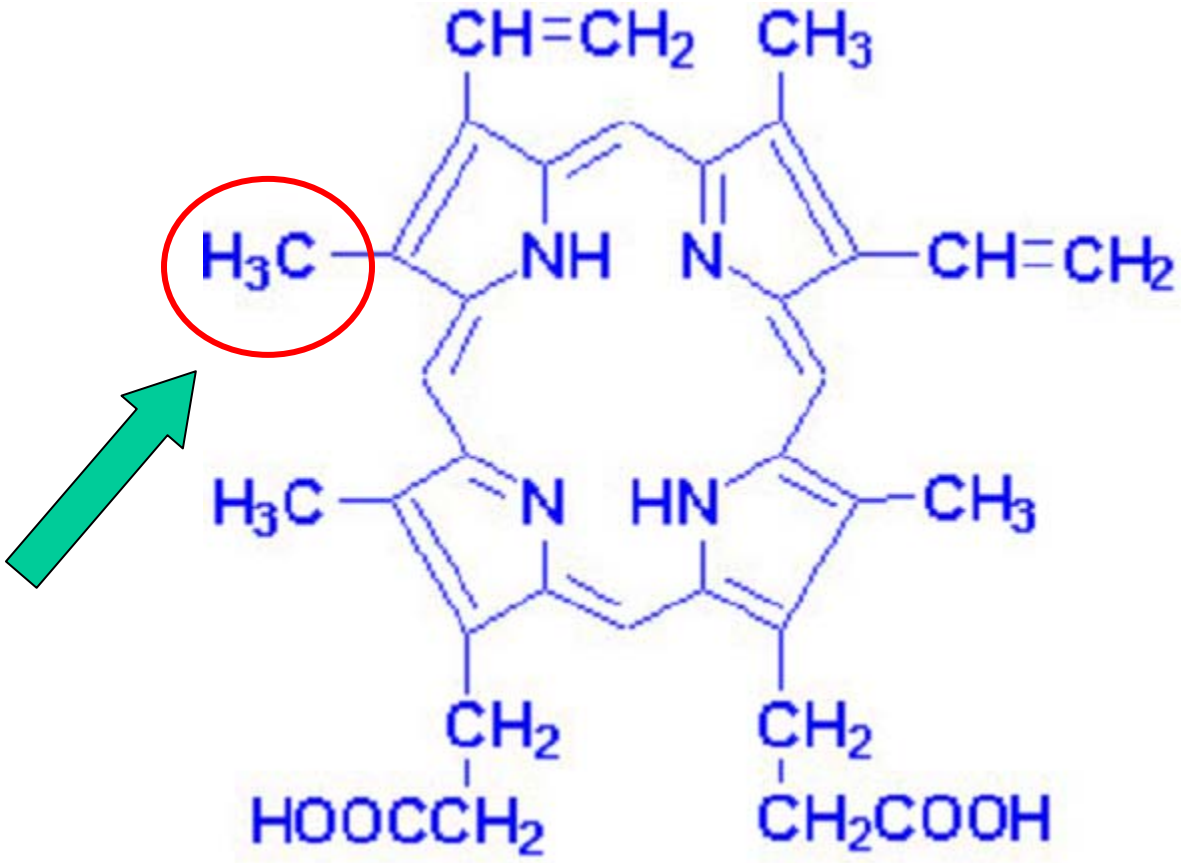
Chlorin in chlorophyll→

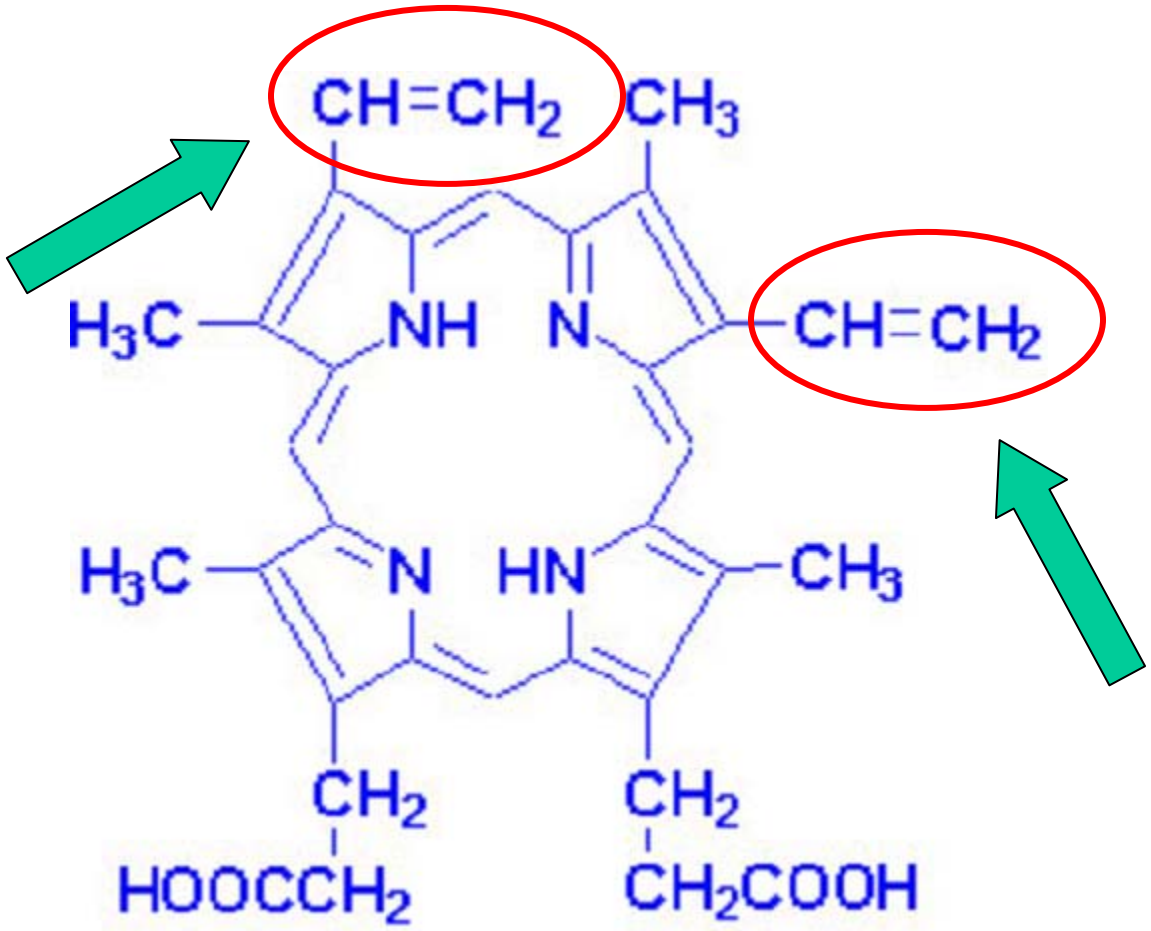


and we must draw what??
PPIX. Only

How to remember how to draw PPIX




CH=CH2
CH3
H3C
NH
N
CH=CH2
H3C
N
HN
CH3
CH2
CH2
HOOCCH2
CH2COOH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H3C
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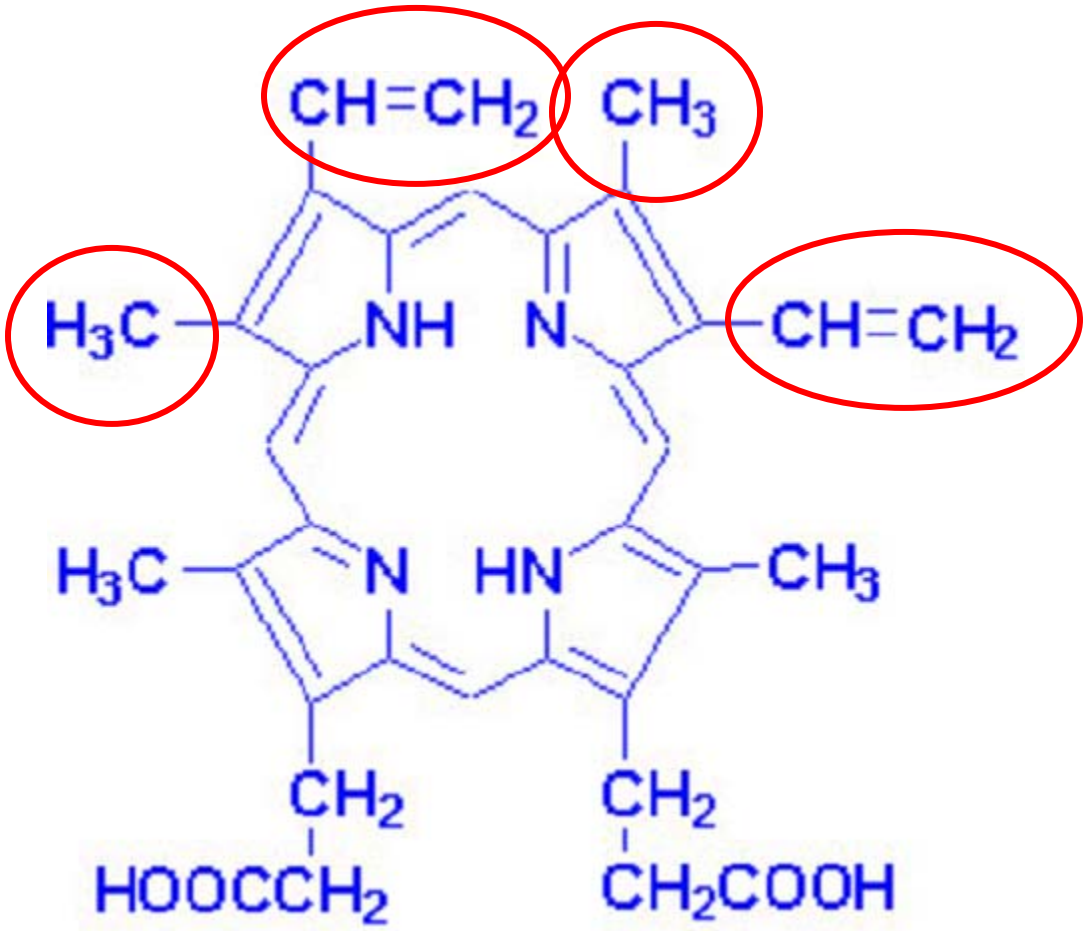
CH2
HOOCCH2
CH2COOH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HN
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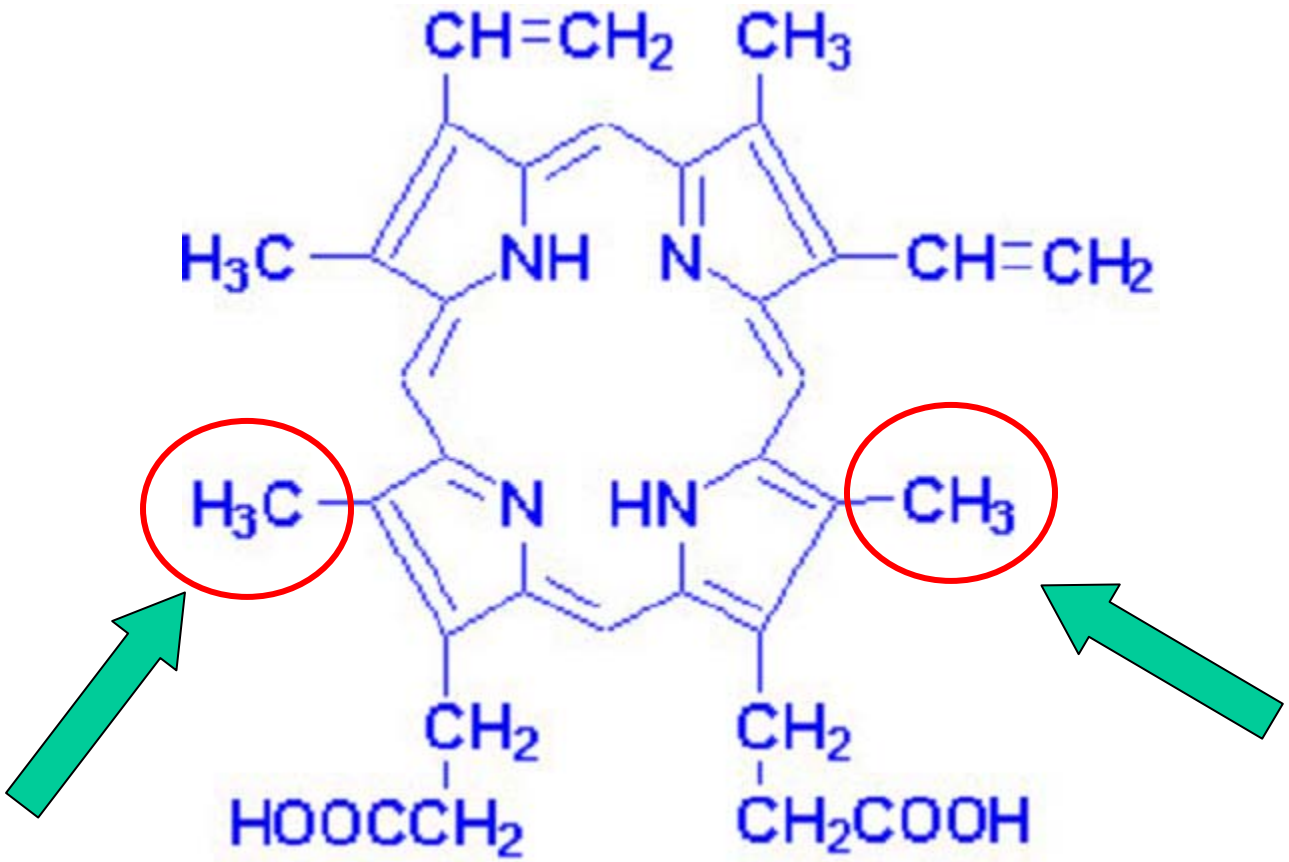
CH2
CH2
HOOCCH2
CH2COOH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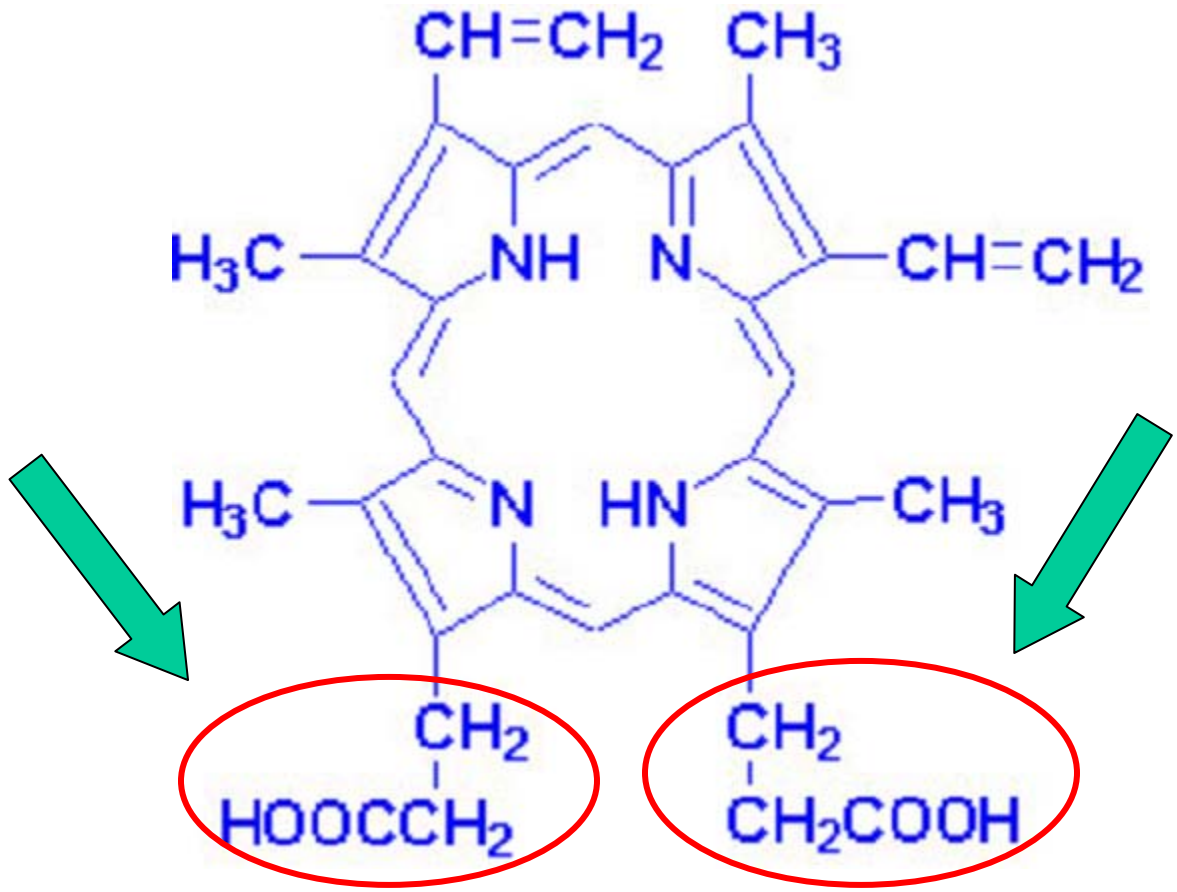
CH=CH2
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CH=CH2
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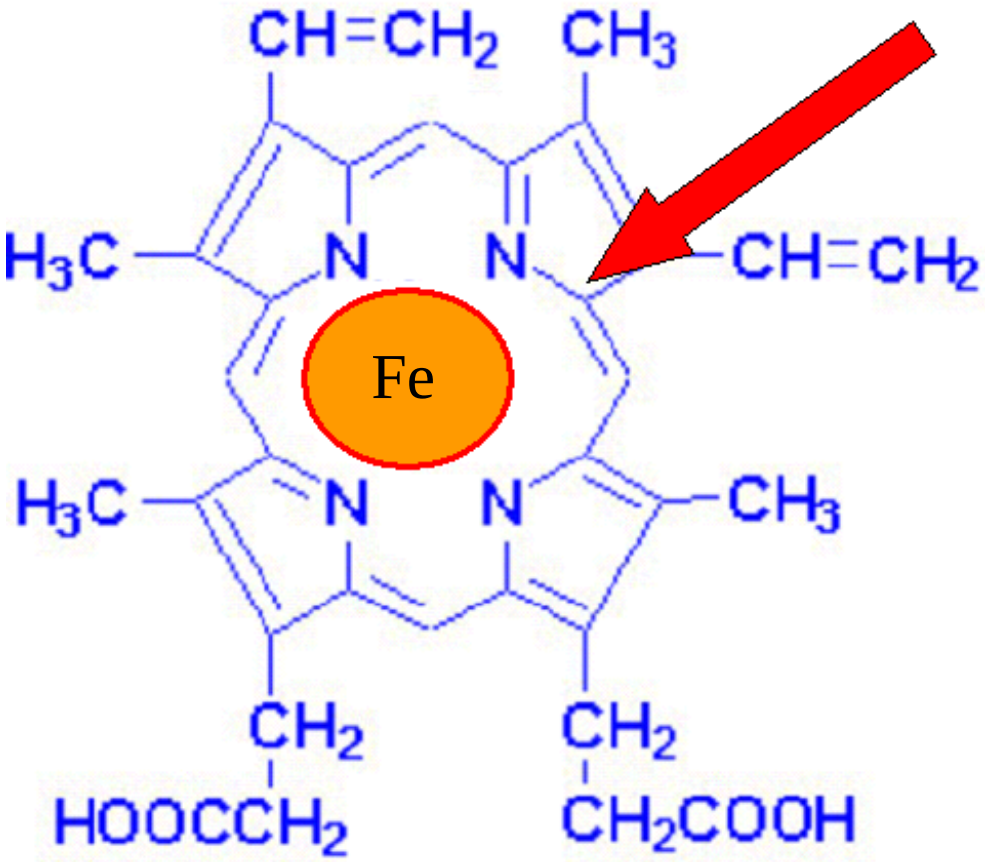
HOOCCH2
CH2
CH2COOH



Iron protoporphyrin IX – usually called 'heme' – Fe can be 2+, 3+ or 4+
Key to heme proteins – see myoglobin, hemoglobin, catalase, and many others – variations in the peripheral groups are found in proteins like cytochrome c. Many here proteins use the imidazole nitrogen (HIS) for the 'proximal', 5th position amino acid. The 6th position is occupied by the 'distal' amino acid, water or a special ligand, like O_2.

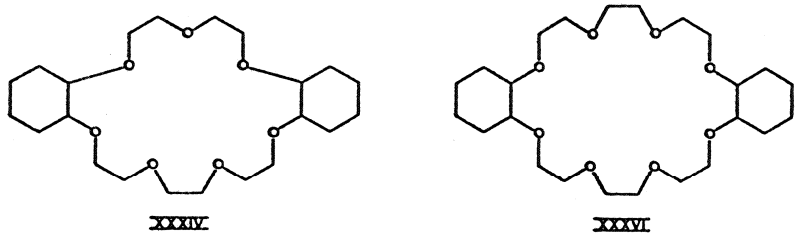
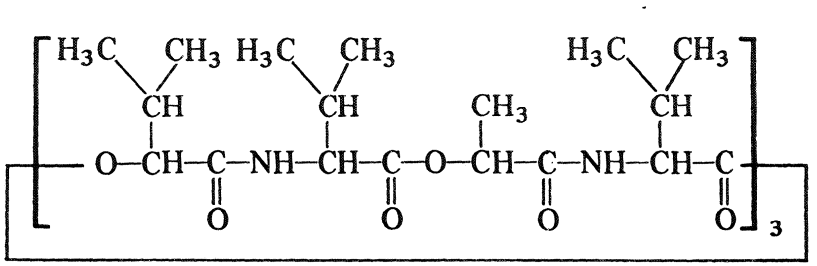


FIG. 1. Cyclic polyethers numbered according to Pedersen (10).



Valinomycin

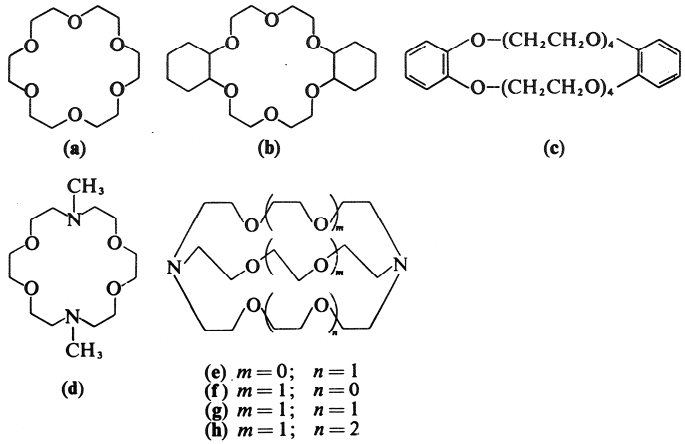


FIGURE 15.5. The structures of synthetic ionophores. [After Lehn, Struct. Bondg. 16, 1 (1973).]

1141

1140
1139

Cyclic polyethers – learn how to recognise polyethers (Fig 1 type – see next slide for more details) – valinomycin, a polyether antibiotic (top RHS) – a cryptand – 3 chains of polyethers (Fig 15.5)

Finally, some more usual Ligands

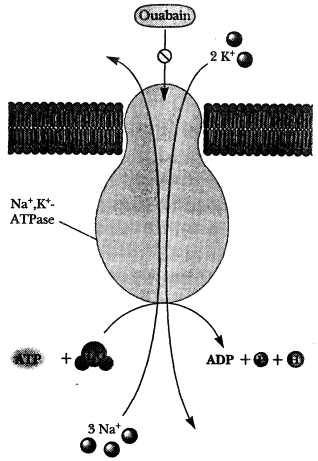
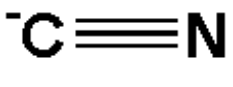
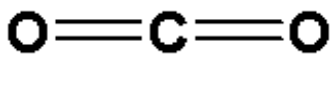


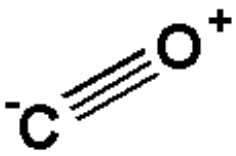
FIGURE 10.8 • A schematic diagram of the Na^+,K^+-ATPase in mammalian plasma membrane. ATP hydrolysis occurs on the cytoplasmic side of the membrane, Na^+ ions are transported out of the cell, and K^+ ions are transported in. The transport stoichiometry is 3 Na^+ out and 2 K^+ in per ATP hydrolyzed. The specific inhibitor ouabain (Figure 7.12) and other cardiac glycosides inhibit Na^+,K^+-ATPase by binding on the extracellular surface of the pump protein.



Cyanide



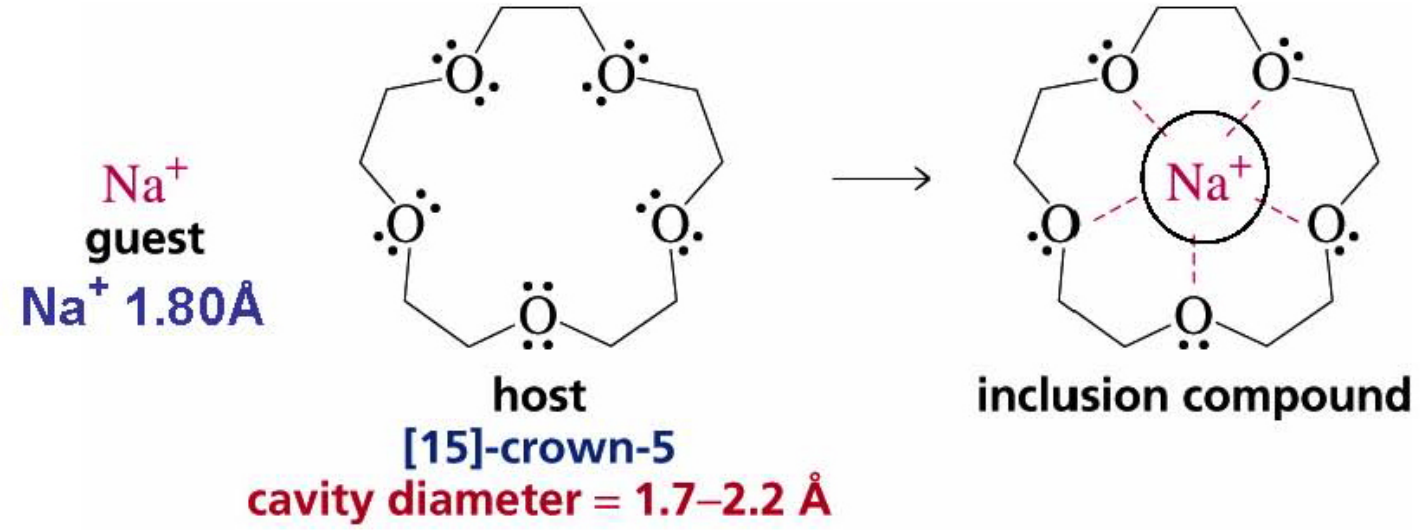
Carbon Dioxide

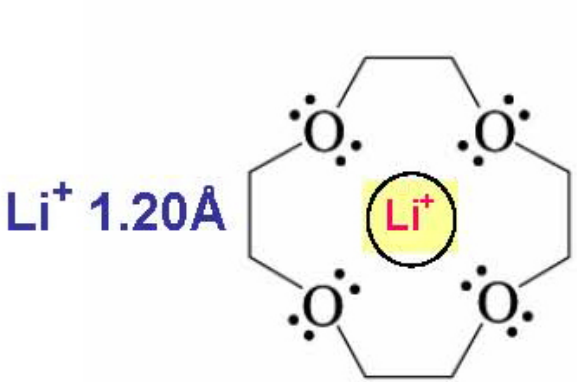


Carbon Monoxide

L-B	R-M	K-S	Problems to do
			If blank – see later

How do cyclic polyethers "crown ethers" work?





Special molecules that bind metals:

Shapes of complexes

1. Forming complexes is the key to many biologically important reactions.
2. In fact even metals not thought to form well-defined complexes (Group 1 & 2), preferring to exist as isolated ions, are always surrounded by water – a shell of 6 – 8 water molecues, and in their biological passage – these molecules are transported often into and then out of of cells, these transporters or pumps have tuned groups to bind to the metals – **hard metals so hard attaching atoms – a good guess would be?**
3. Group 1 and 2 metals maintain osmotic pressure across membranes, this same atom is part of an enzyme molecule used to move these metals through a lipid bilayer that is the membrane.
4. On the other hand, the dBMs are always coordinated to something – being transported or functioning. The chemical nature of the attached ligands and the shape **control function.**
5. We are interested in:
    a. The possible shapes of complexes that form
    b. The atoms that bind the metals and the molecule that inludes those atoms – the ligands
    c. The effect this shape has on the atomic orbitals of the coordinated metal – most significantly, the effect on the 5 3d orbitals of the dBMs
    d. The binding constants, the K_F, showing especially the relative bind strengths. (In a competition, the metal with the greater K_F will win the ligand!)
    e. The form of the ligand depends on its state in acidic, neutral and basic conditions, this is controlled by pK_a.

L-B	R-M	K-S	Problems to do
22 33			If blank – see later

Shapes of complexes

We are most interested in

1. Coordination Number (CN)
2. 4 tetrahedral TET and sq planar SP
3. 5 sq based pyramid SBP
4. 6 octahedral OCT

Examples:

CN=4 Zn(II) in CA*

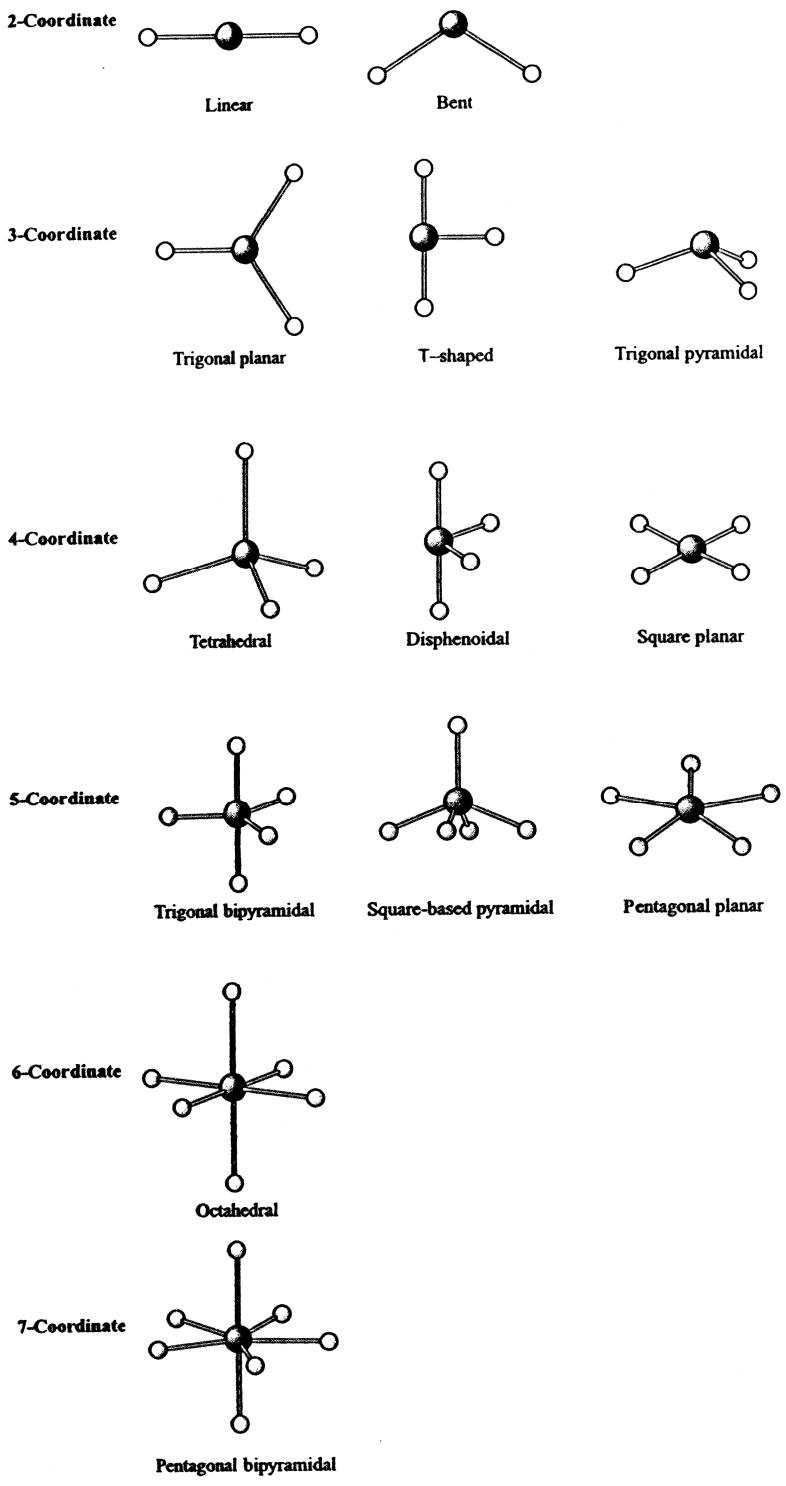
CN=5 – deoxy myoglobin

CN=6 - oxymyoglobin

*CA: carbonic anhydrase – see Zn unit coming

.

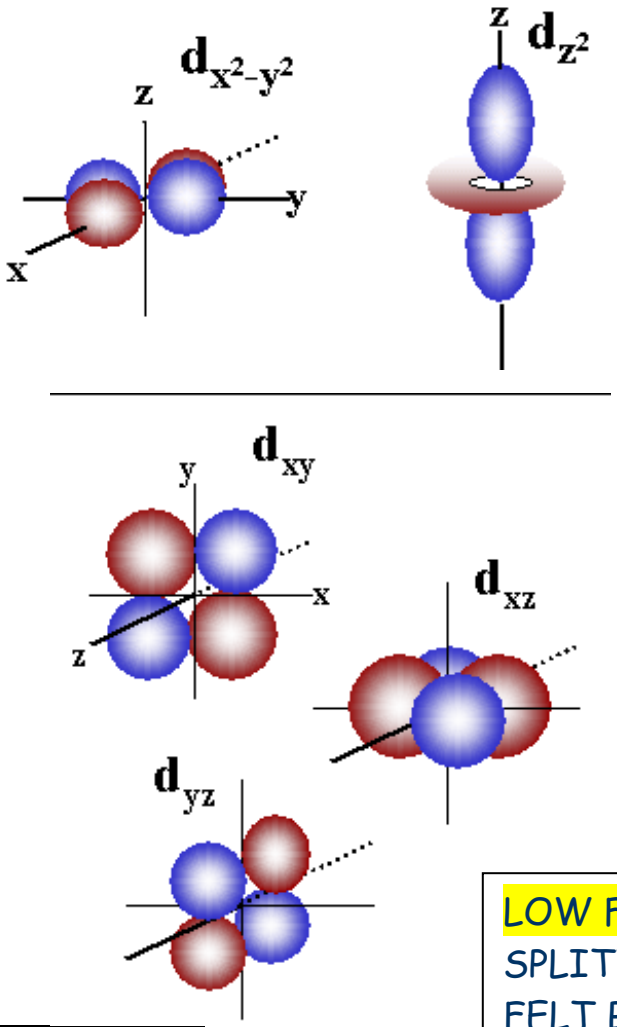
L-B	R-M	K-S	Problems to do
33			H&S 2nd Ed- p 45-49. Know the shapes – no need to learn molecules NOT in 211a lecture notes.



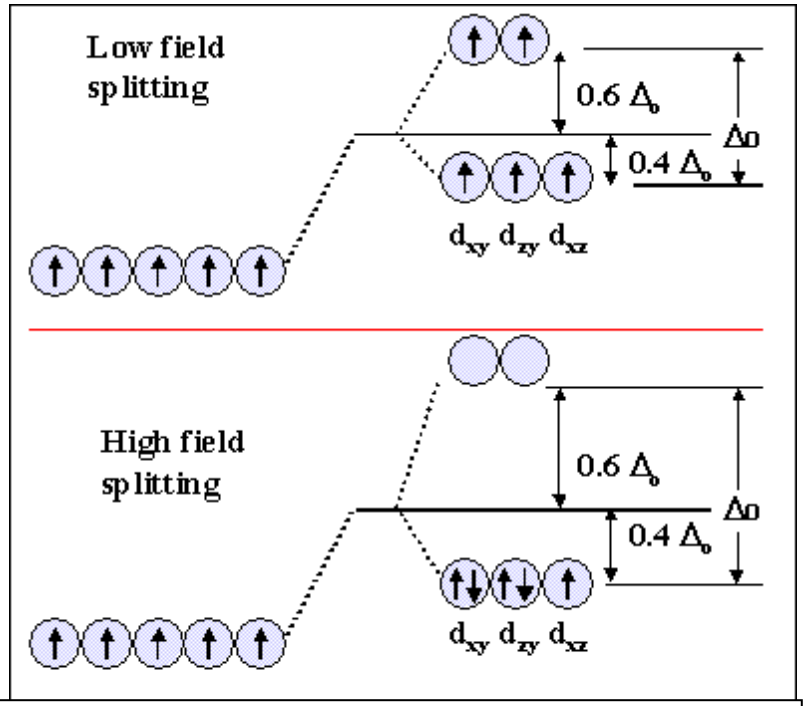
Special molecules that bind metals

Effect the shape of a molecule (the geometry) has on the energies of the 5 3d orbitals – refer to crystal field splitting diagrams and the spectrochemical series here.

This is for Fe(III) – ferric iron - $3d^5 4s^0$



LOW FIELD = WEAK FIELD
HIGH FIELD = STRONG FIELD



LOW FIELD = WEAK FIELD – NOT ENOUGH SPLITTING TO OVERCOME THE REPULSION FELT BY ELECTRONS WHEN THEY PAIR UP CALLED – HIGH SPIN (MORE UNPAIRED ELELCTRONS = MORE SPINS)
HIGH FIELD = STRONG FIELD – SPLITTING ENERGY EXCEEDS REPULSION – SO ELECTRONS PAIR UP. CALLED LOW SPIN
See next page …

L-B	R-M	K-S	In Housecroft 2nd ed.	Problems to do
1-2 34;35		29;30	Ch. 20, p 557-564.	

Effect of ligand field strength on the splitting of the 3d orbitals.

Weak field ligands

1. Strong field ligands

2. Why is this important for us to understand?

3. Myoglobin & Hemoglobin

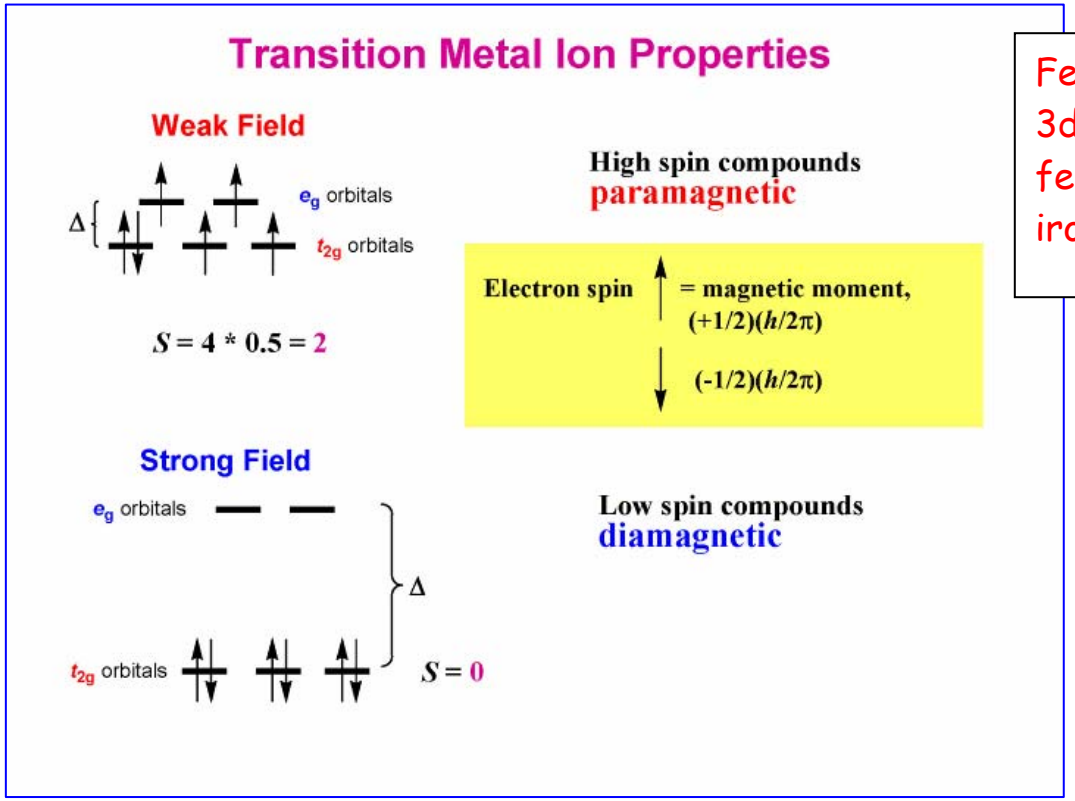
4. There is a theoretical basis – not for us in detail – just 4 examples, "The Spectrochemical Series"

5. Weak field: fluoride, hydroxide – intermediate: water and oxides, RO^-,- Strong field: cyanide, carbon monoxide

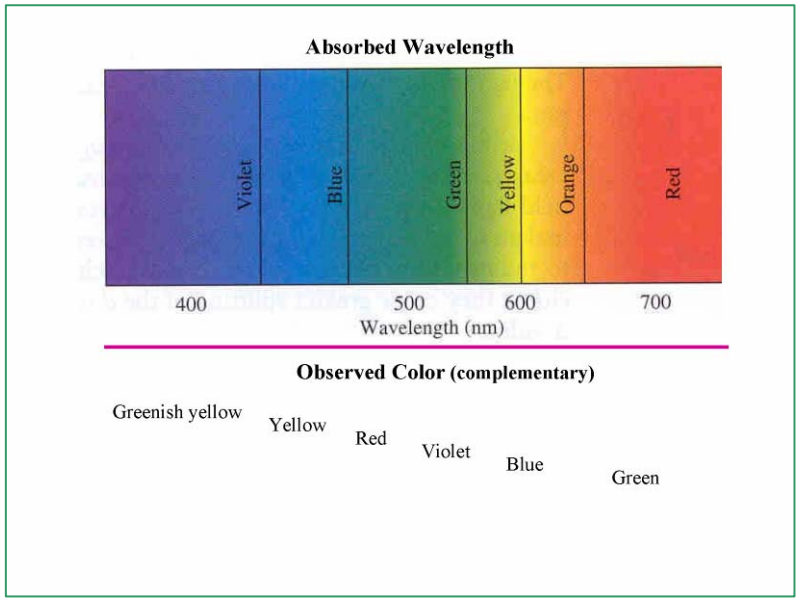
6. (H&S p 559)

7. What does all this have to do with biological molecules? Well, the field strength controls the availability of electrons and whether the molecule is going to be DIAMAGNETIC OR PARAMAGNETIC – and we will see this in the colours. Paramagentic metals are a problem in biology = RADICALS.

L-B	R-M	K-S	Problems to do
288 - Hb			If blank – see later



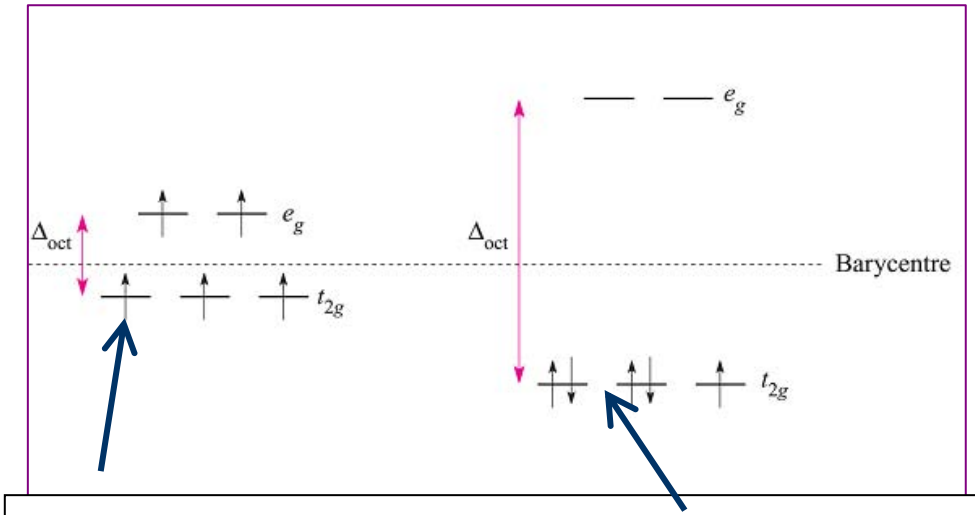
Fe^{2+}
$3d^6$
ferrous
iron

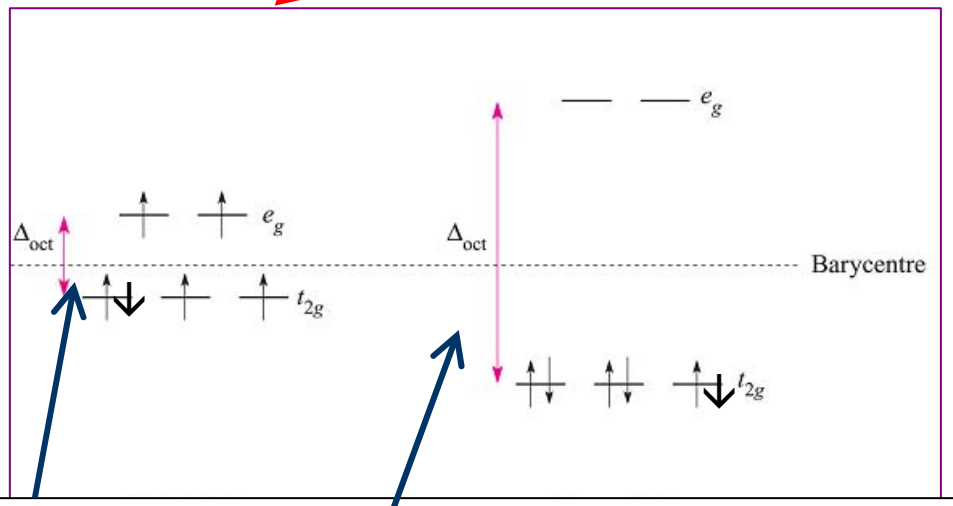


For us: Fe(III) has 5 3d electrons: $3d^5$ and is always paramegntic whereas Fe(II) has 6 3d electrons and is only paramagentic when high spin. Low spin is always diamagnetic

For Fe(II) – add 1 electron! To make 6 here

This is Fe(III), only 5 3d electrons





Weak field (F^-, OH^-, intermediate H_2O and also 1 N from HIS plus H_2O)

Strong field CN^-

Weak field (2 x H_2O and also 1 N from HIS plus H_2O)

Strong field – dioxygen with HIS-N in 5th position and His-N plus *CO*

Fe(III) always unpaired electrons, therefore, always paramagnetic

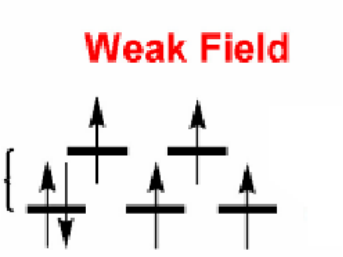
Fe(II) only paramagnetic if high spin – low spin is diamagnetic

The Spectrochemical Series (for Chem 2211a)

Weak F^- OH^- RO^- (RCOOH) Int H_2O NH_3 Strong PPIX-4N's O_2 CN^- *CO*

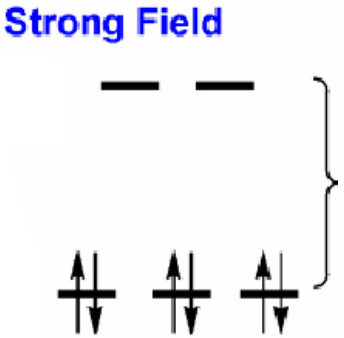
A quick (very quick) primer in the dioxygen chemistry of hemoglobin – see p 40 of the Inorganic Notes for more details and the text books.

1) DEOXYhemoglobin (in the veins and returning to the lungs) has 1N from imidazole (proximal, or 5th position), 4 N's from the protoporphyrin IX ring (the heme ring) and nothing in the 6th position or distal position. Because of this (5-coordination not 6 = Weak Field) the 6 electrons in Fe^{2+} adopt a High Spin electronic configuration ($5x+\frac{1}{2} + 1 \times (-\frac{1}{2})$ =sum of spins= 2).



High Spin Fe^{2+} is larger than Low Spin Fe^{2+} so does not fit into the hole in the heme ring – the ferrous ion pops out of the ring a bit on the side of the proximal histidine.

When oxygen binds – this makes the OXYhemoglobin and the 6 coordination exerts a Strong Field, the energy gap between the top 2 and the bottom 3 3d orbitals increases, and the electrons pair up = Low Spin configuration (S=3 x $+\frac{1}{2}$ + 3 x $-\frac{1}{2}$ = S=0).. Low Spin Fe2+ IS SMALLER THAN High Spin Fe2+ so the ferrous iron moves back into the plane of the ring.



How does all this movement control oxygenation? Well, there are four hemes in hemoglobin, and they are all connected through a hydrogen bond network. When the Fe drops out of the plane it pushes the Histidine down, this mechanically moves the protein. So, all the other hemes 'know' that one heme is not in the DEOXY-or sprung state. Conversely, when the Fe picks up the dioxygen, movement back into the plane pulls the attached Histidine and 'tells' the other hemes that it is now oxygenated. This 'spring-loaded' effect also has the property of delaying oxygenation until there is plenty of dioxygen available – so all 4 heme groups can pick up oxygen at once and then travel fully oxygen-loaded to the muscles.

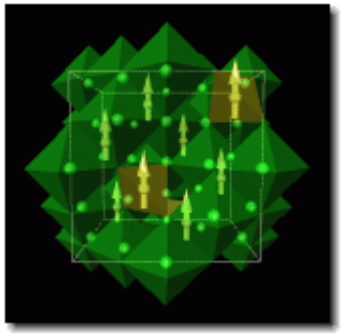
Magnetism in biology …

Thought to be the way that birds and fish migrate .. lining up with the earth’s magnetic field.

‘Magnetitie’ crystals are small magnets.

Fe_3O_4 – ‘iron oxide’ magnetite - really $FeO.Fe_2O_3$ – that is two types of iron, Fe(II), and Fe(III). .

The Fe(III) is the ‘magnetic’ bit.



Magnetic particles in the lateral line of the Atlantic salmon (*Salmo salar* L.)

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SUMMARY

Magnetization measurements with a superconducting quantum inference device magnetometer of various tissues of the Atlantic salmon (*Salmo salar* L.) have shown the presence of magnetic material associated with the lateral line. The data suggest that the material is magnetite and of a size suitable for magnetoreception. Magnetic particles were isolated from the lateral line and nerve tissue, which have characteristics suggesting that the material is magnetite and of biogenic origin. The magnetic particles and their association with the lateral line are discussed in relation to their possible role in allowing the salmon to orientate with respect to the geomagnetic field during the high-seas phase of their migration.

1. INTRODUCTION

A variety of organisms such as bacteria (Blakemore 1975), honey bees (Lindauer & Martin 1968), birds (Walcott & Green 1974; Beason & Nichols 1984) and sea turtles (Perry *et al.* 1985) are sensitive to the geomagnetic field and may use it as a navigational aid. The tissues of many of these species contain biologically deposited particles of magnetite, suitable for use in magnetoreception. In teleosts, magnetite has been detected predominantly in the region of the ethmoid tissue (Walker *et al.* 1984; Kirschvink *et al.* 1985; Walker *et al.* 1988; Mann *et al.* 1988). However, ultrastructural studies have not shown that the magnetite is innervated or associated with an existing receptor system. This paper describes the presence of magnetic material, probably magnetite, concentrated in the lateral line of the migratory Atlantic salmon (*Salmo salar* L.). The size and number of the magnetic particles are sufficient to allow the salmon to detect the geomagnetic field. It is suggested that the particles may have a navigational role during the high-seas migration of the salmon.

2. MATERIALS AND METHODS

(*a*) *Magnetic measurements*

Seventeen salmon (11 smolts and 6 adults) were examined for the presence of magnetic material. To exclude magnetic contamination, tissue samples were dissected from each fish by using glass microtome knives in a clean laboratory (Walker *et al.* 1985). Each sample was weighed, washed in glass distilled water and packed into plastic cylindrical pots (14 mm diameter, 9 mm high). After freezing in liquid nitrogen, plugs of tissue of consistent size were extracted. Tissue samples examined included the eye, skin, ethmoid tissue, brain, muscle and an area containing the lateral line and nerve. Magnetization measurements were made with a superconducting magnetometer (SHE Model BMP with rf superconducting quantum interference device (SQUID)). Initially, the natural remanent magnetization of all the samples was measured. Subsequently the saturation isothermal remanent magnetization (SIRM) was measured immediately after exposing each tissue sample to a unidirectional magnetic field of 0.7 T. Coercivity spectra were then obtained for the lateral line and nerve tissue of an adult salmon by subjecting the samples to progressive isothermal remanent magnetization (IRM) acquisition and alternating field (Af) demagnetization in fields ranging from 2–700 mT.

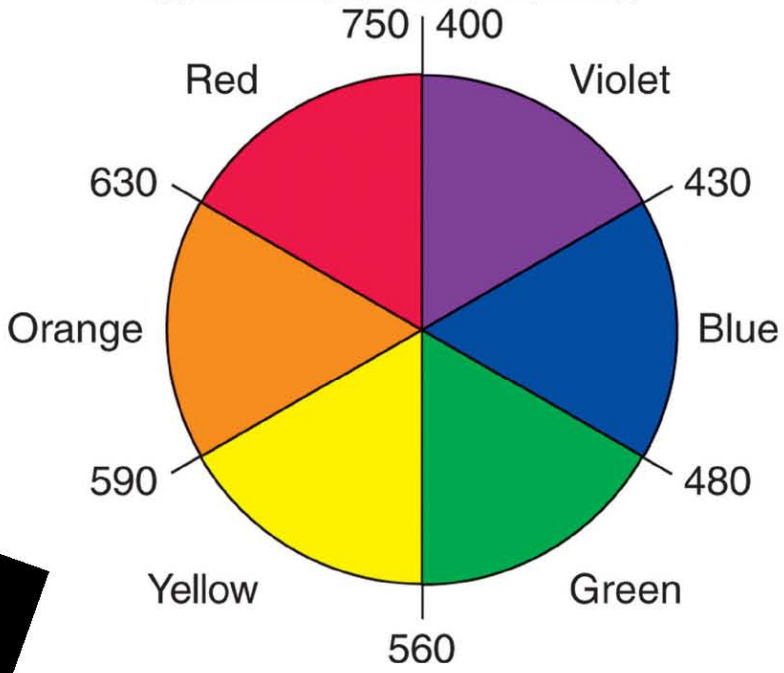
(*b*) *Extraction of magnetic material and electron microscopy*

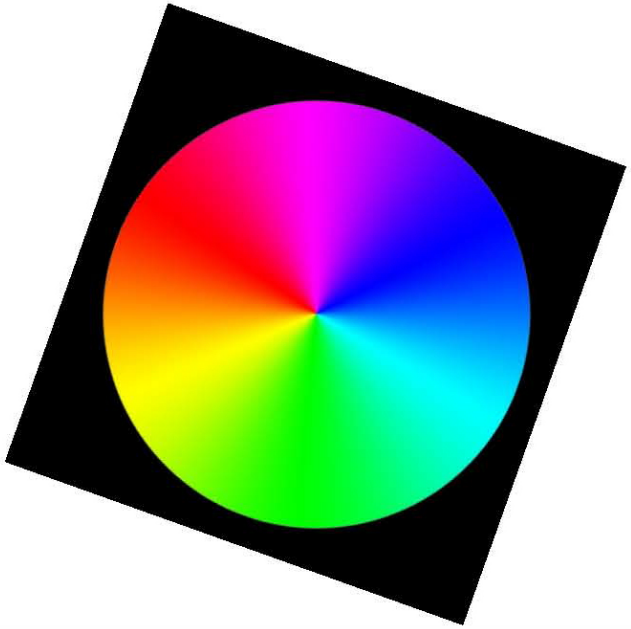
Magnetic material was extracted from the lateral line and nerve tissue of several adult salmon by using a technique similar to that of Walker *et al.* (1985). Tissue was ground with glass-distilled water in a glass tissue grinder. Released oil and fat droplets were removed by adding anhydrous ether and decanting. The residue was centrifuged and digested with 5% Millipore-filtered hypochlorite solution. After digestion, the residue was repeatedly washed and centrifuged, and then resuspended ultrasonically. The magnetic material was concentrated at the side of the test tube by using a high magnetic field produced by a rare earth (iron–neodynium boride) magnet wrapped in heatshrink plastic. The final extracts of the particles were prepared for observation under the transmission electron microscope (TEM) by pipetting the material, in suspension, onto carbon-coated copper grids and allowing the sample to evaporate to dryness.

The magnetic extracts were then viewed with a Jeol 300 CX electron microscope at magnifications of

What else changes as a function of the oxidation state of dbMs?

1) The coordination number (CN)
2) Therefore, the shape
3) The colour of the compound →
4) The magnetic properties





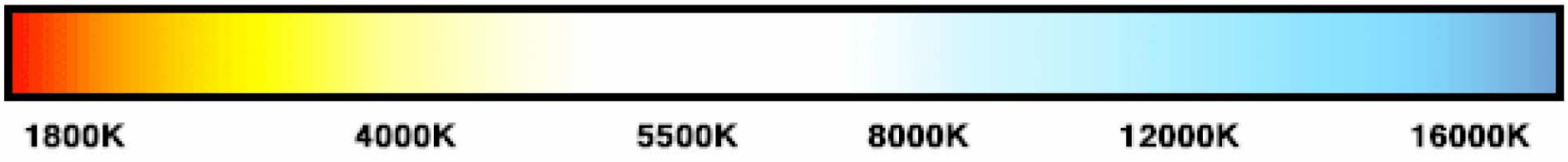
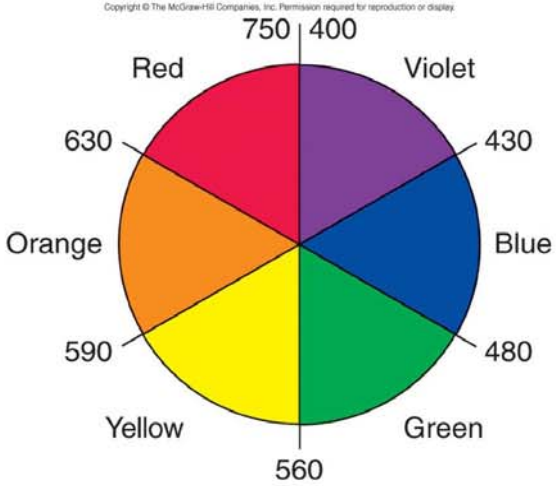


Table 23.11 Relation Between Absorbed and Observed Colors

Absorbed Color	λ (nm)	Observed Color	λ (nm)
Violet	400	Green-yellow	560
Blue	450	Yellow	600
Blue-green	490	Red	620
Yellow-green	570	Violet	410
Yellow	580	Dark blue	430
Orange	600	Blue	450
Red	650	Green	520

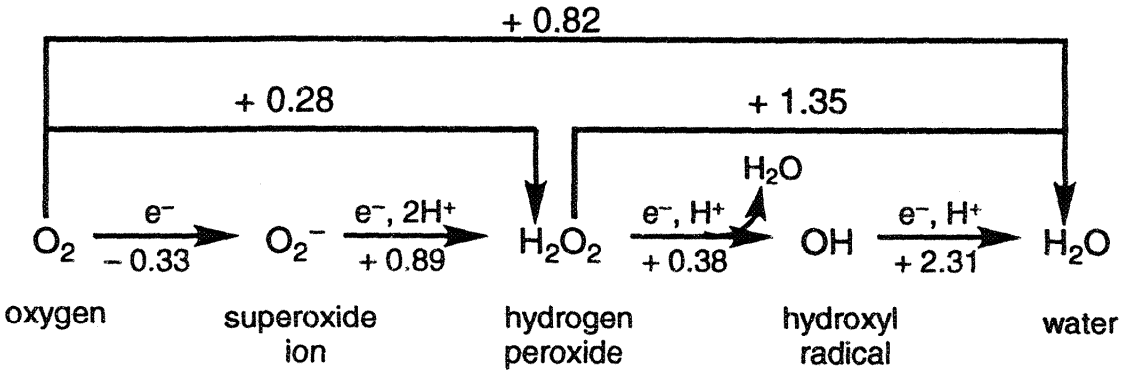


The most important ligand and molecule – OXYGEN

1. First because oxygen in its many forms dominates mammalian existence we need to look at how these different forms are interconnected.

2. The electrochemical potentials are only ½ of the reaction. A second molecule or atom must be connected – the sum of the ½ potentials must be positive for that combination to react.

3. Electrochemical potentials are thermodynamically controlled – there is no information on the rate of the reaction – luckily! Why luckily? Consider what humans are made of and the composition of gas surrounding us…



Which biological molecules are involved with the oxygen species shown here?

(Cu, Zn) Superoxide dismutase (SOD) – breaks up O_2^{--} —to H_2O_2
(Fe(III)-Fe(IV))Catalase – breaks up H_2O_2 – to O_2 and H_2O

(Fe(II)) Hemoglobin – transports O_2
(FE(II)) Myoglobin – stores O_2

L-B	R-M	K-S	Problems to do
6-7 284-302 – Hb, but esp. 287 325 O_2^-			Which biomolecules are specifically involved with O_2, O_2^-, and H_2O_2 ? Which metals are involved?

Luckily, because ...

(remember how you used to play with matches .. why did that work? Now you try to avoid setting the kitchen on fire at night, why does that happen,

so, lipids + oxygen = CO_2 and H_2O plus ..)

Meanwhile, continuing with the course, we’re still interested in ...”Important chemistry and special inorganic chemistry for bioinorganic chemistry”

And will consider now ..

Equilibrium constants K_F

Chelate effect

K’s for multiple Ligands

pK_a

from the overhead …

L-B	R-M	K-S	Problems to do
			If blank – see later

Expectations from the material in this unit	
1	Know your way round the Periodic Table – esp elements of bio-interest in Groups 1, 2, 14-17. Which are these elements? What are the configurations of the row 2 and 3 metals we are interested in? Know the orbital shapes and labels s, p, and d What is special about the ionization energies across the rows? How does this change the characteristics of the element wrt forming compounds? What happens to the size of elements when oxidized? Reduced? What is a ligand? How is it defined? Why do the hard metals lie on the LHS of the Periodic Table? And the soft metals are? And the hard ligands? And the sift ligands? What are the distinguishing features of all these types of species?
2	Predict good ligand atoms for the following dications**: Zn, Cd, Hg – which amino acids would be prime targets? And Mg, Ca – what about Pb? (See ch. 17 in K&S) **what does this mean?
3	What is BAL? Why was it used in the 1st and 2nd World Wars? What is the L in BAL? What is EDTA? What does it bind best? Why? And, deferrioxamine B – what is it? Why would you be given this as a drug? What is special about the polyether molecules? How would they 'work' in a biological system? Match the following metal ions to the preferred amino acids: K, Zn, Cd, Cu as +1.
4	Identify those amino acids most likely to bind metals – which atoms bind directly to the metal in these molecules? Be able to draw and recognise protoporphyrin IX
5	How do the 3d orbitals split? What effect does this have on the arrangement of electrons? Which of the compounds of oxygen shown in slide 1079 are important to an organism? Which would be toxic? See R-M p 205 for a start on this

Study questions from the lectures to date and from the books (S-L; R-M; K-S)	
Lectures	Using LB or other book and lectures – explain how dioxygen binding takes place in the heme protein myoglobin in terms of the 3d orbitals and d electron configuration Equilibrium questions to come with the 'overhead' lecture unit.
L-B Do questions: – p 40 1-3; – p 136 1; 2; 4 – p 170 1, - just the active site design;	Ch 2 – p 21-40; As in lectures – check out p 23; 3d – shapes: 33; 32- ox states – know Gr 1 & 2 – Fe, Co, Cu, Zn; 34 – 35; what is the oxidation state on the Fe's in Fig 9.2? See how Mb works – p 288 – know the 3d splitting pattern for both situations; Ligands: 25; 39; what is different about the porphyrin ring in Fig 9.5 and 9.6 cf heme in myoglobin? HS: 23; classify each amino acid p 44 – H, S, not either; see p 46 P 51 – what are the ligands & Fe ox states? Explain the choice of ligands for Pb and Pt p 67; explain the ligand choice in Fig 5.3 p 109; And on p 120-125; what about on p 130? What is the ox state – why does this help your explanation? Explain ligands on p 133 – be able to draw ; Know the cmpd on p 141 – but only schematically – explain bonding pattern; account for the Zn binding in p 179 and Mg in p 195; Account for the Cu binding site in Fig 9.4; The Zn in Fig 10.1 –what's interesting about this cf our notes? See the Zn in p 262 – this is 'normal'; What is special about the way Zn works in carboxypeptidase – p 265? Nature chose this method again in AP – p 268;
R-M	3d – p 13-16; see how O_2 might bind – p 165 and p 166 FeS enzymes – see p 240 for the oxidation states of the Fe – why is it difficult to reconcile the ligands and metals with the HASB theory?

Housecroft and Sharpe 2nd ed. On 2hr loan	Bio examples- check out the metal-ligand pairs – do they obey the HASB rules? Fig 28.3; 28.4; 28.22; qu. 28.28.15, and 28.22 on p 861; Equilibrium Constant calculations – K and Beta : see p 180 – 186 – has K, ΔG and ΔS text – follows MJS lectures closely. Do, Self-Study on p 181; Follow Worked Example 6.6 (p 182); Do Self Study 1, 2 and 3 - see end of p 185 and top 186 for entropy discussion. Do Questions on p 190 & 101: 6.1; 6.13; 6.20; 6.25; 6.29(b); 6.32..
K-S	3d orbitals- p 30 and 31 – how O_2 binds to Fe – 88 - Ligands – p 32 – O2 p 87 - ; 274 polyethers and cryptands – be able to recognise naming method – but not be able to name one; 276; p 289 – what is the molecule? How do we usually draw it?- be able to draw this molecule; HSAB – identify the ligands – explain why they fit the metal – p 129 – 154; 158; 189; 247 & 249 – look up on the Internet for better picture – what does CA do?; 252 – check the Internet for better picture of carboxypeptidase; 276; ; 296 – what are the ligands actually? OK – so none of you believed me about magnetic salmon – see p 315 – what is the core of the mineral in magnetic bacteria?